FDA REGULATION OF SOFT CONTACT LENSES

HEARING

BEFORE THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

OF THE

COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE

HOUSE OF REPRESENTATIVES

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FDA REGULATION OF SOFT CONTACT LENSES

FRIDAY, DECEMBER 12, 1980

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS,
COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE,
Washington, D.C.

The subcommittee met, pursuant to notice, at 10 a.m., in room 2237, Rayburn House Office Building, Hon. Albert Gore, Jr., presiding (Hon. Bob Eckhardt, chairman).

Mr. GORE. The subcommittee will come to order.

On July 1, 1980, the Subcommittee on Oversight and Investigations conducted a hearing on the Food and Drug Administration's—FDA—regulation of the soft contact lens industry.[1] At that hearing we heard highly questionable testimony from a medical officer of the FDA. Moreover, we learned that consumers were forced to spend well over $200 million per year in additional expense because salt tablets used to rinse soft contact lenses were removed from the market without scientific justification and replaced with a much more expensive preserved saline solution.

We were told the reason salt tablets were removed from the market was because of the safety problems they posed to the consumer. To justify this action, the FDA's chief medical officer in this area, Dr. Arnauld Scafidi, presented to the National Registry on Ocular Side Effects a listing of 200 adverse reactions reports that he claimed to have collected.

The subcommittee reviewed the medical officer's compendium of adverse reactions reports and raised a number of serious questions regarding the authenticity of the reports. It is worth noting that these adverse reaction reports were characterized in testimony by the Director of the Bureau of Drugs as being of questionable scientific credibility.

In addition, the subcommittee found that Burton-Parsons, the manufacturer of the only solution to replace salt tablets—who therefore gained substantially from the removal of salt tablets—established a close personal relationship with the two FDA employees most instrumental in having the tablets removed from the market, Dr. Arnauld Scafidi and Mary Bruch, a microbiologist.

We will ask the commissioner of the FDA, who will testify today, what action the FDA has taken to expunge from the National Registry the reports filed by Dr. Scafidi and what action the agency has taken to counteract the current misleading advertising and other promotional material describing salt tablets as unsafe.

[1] See hearing "Soft Contact Lens Solutions: Oversight of FDA," Oversight and Investigation's Subcommittee of the Committee on Interstate and Foreign Commerce, July 1, 1980, Serial No. 96-187.

Our hearing today is a follow-up to our last hearing. On this occasion we will review a situation involving FDA's approval of a soft contact lens for a soft contact lens manufacturer. In this connection we have asked Automated Optics, another and competing manufacturer of contact lens polymers, to explain its experience with the FDA.

We will discuss with the commissioner of FDA and FDA bureau and division managers the possibility of false statements being filed by the product applicants and the failure of FDA to take action against this applicant.

We will also explore whether or not FDA's failure to properly monitor this prospective applicant is again tied to the relationship established between Burton-Parsons and officials of FDA.

I will call now on our minority member for the hearing, Mr. Corcoran.

Mr. CORCORAN. Thank you very much, Mr. Chairman.

I also want to welcome our witnesses here this morning. Because of a conflict with another subcommittee which is meeting on which I am privileged to serve, I will not be able to be with you for the entirety of the hearing, but I would like to express the same concern that our chairman this morning has expressed, and that is, we are all concerned here in the Congress that every party before an agency of the Federal Government would be afforded due process of law.

I was able to participate actively in our earlier hearing and hopefully this hearing will tend to clarify whether or not that has been the situation over at the Food and Drug Administration involving the particular problem that has justified the two hearings now that our oversight committee has held on this matter.

I am hoping that we can get more clarification so as to make a determination later on whether or not additional oversight hearings as well as perhaps some additional legislative action might be required in order to clarify the situation and make certain that this kind of problem does not occur in the future.

Mr. GORE. Thank you, Mr. Corcoran.

We have two panels of witnesses today. I would like to call now the first panel, which consists of Mr. Robert Spriggs, president of Automated Optics, from Clearwater, Fla., and his counsel, Norman Stepno and Dave Brown.

If you gentlemen would come forward, please. If you would remain standing and raise your right hand, all three of you, please.

Do you solemnly swear that the testimony you are about to give is the truth, the whole truth and nothing but the truth, so help you God?

Mr. STEPNO. I do.

Mr. BROWN. I do.

Mr. SPRIGGS. I do.

Mr. GORE. Please be seated.

Welcome. We appreciate your willingness to come and assist this subcommittee in its investigation of the matter.

Mr. Spriggs is on our left, Mr. Stepno and Mr. Brown are on the right.

Do any of you have an opening statement that you would like to present?

TESTIMONY OF ROBERT G. SPRIGGS, PRESIDENT, AUTOMATED OPTICS, CLEARWATER, FLA., ACCOMPANIED BY NORMAN H. STEPNO, ATTORNEY AT LAW, BURNS, DOANE, SWECKER & MATHIS, ALEXANDRIA, VA., AND DAVID BROWN, COUNSELOR AT LAW, SHAPIRO & BROWN, GARDEN CITY, N.Y.

Mr. STEPNO. Yes, Mr. Chairman.

My name is Norman Stepno. My background is biochemistry; I have also had roughly 15 years' experience in the polymer field. I too am a lawyer and represent Automated Optics.

Mr. GORE. Please proceed.

Mr. STEPNO. I am also a very confused lawyer this morning, Mr. Chairman, confused because of certain treatment that has been accorded my client before the FDA vis-a-vis certain treatment that was accorded the company called Soft Lenses, Inc., a licensee of Automated Optics, before the very same people at FDA, and indeed before Mrs. Mary Bruch and Dr. Arnauld Scafidi, mentioned in your opening statement.

What I would really like to do is give you a little bit of background of the soft contact lens industry, our exposure to it, and what happened before a particularly fateful meeting for Automated Optics at the FDA in February 1978.

Soft contact lenses originated in Czechoslovakia, invented there by Dr. Otto Wichterle in the late fifties and early sixties. I have traveled to Czechoslovakia; I have taken Dr. Wichterle's deposition; I met with Dr. Wichterle several times in this country since 1974; I have myself prepared hydrophilic polymers for making soft contact lens, and even tried on occasions to shape a lens from that particular polymer—unsuccessful as that was.

After the soft contact lens was developed in Czechoslovakia, a U.S. company heard of this development through the trade literature. That company was National Patent Development Corp. out of New York City. They traveled to Czechoslovakia, met with Professor Wichterle and the Czechoslovak Academy of Sciences where Professor Wichterle was employed. This culminated in National Patent being granted an exclusive license, initially restricted to the United States, for the ultimate marketing here of a soft contact lens product.

National took this license back to the States and ultimately was successful in exclusively sublicensing Bausch & Lomb. After considerable testing, both manufacturing techniques and testing on the actual lens produced, Bausch & Lomb received the first FDA approval of a soft contact lens product. I believe that was in 1971.

I will refer to the Wichterle-type polymers that went into this first generation soft lens as simply a first generation lens.

Shortly after the Bausch & Lomb impact in the United States, and indeed while they were still in the throes of obtaining their approval at FDA, a second generation lens was developed. This was an American lens. It was invented by one Maurice Seiderman of Hollywood, Calif. The key to the Seiderman lens, rather than the Czech lens, was the inclusion of a certain material or comonomer called N-vinylpyrrolidone. N-vinylpyrrolidone is a very characteristic hetrocyclic nitrogen compound which was copolymerized with the "hema" material utilized in the Czechoslovakian lens.

Mr. Spriggs, on my right here, the president of Automated Optics, heard of the Seiderman development. He traveled to California and after considerable negotiations entered into an agreement whereby he would acquire all of the rights to the Seiderman material. Automated was a small company; they did not have the resources to themselves manufacture a contact lens product so they built a white room in Denver, Colo., for the sole purpose of manufacturing soft contact lens buttons.

A button is simply a chunk of plastic out of which a soft lens is machined, virtually on a jeweler's lathe. It is a lathing techinque.

With this facility onstream, and with an FDA-approved drug master file, Mr. Spriggs was successful in licensing four companies to be business partners of his, who themselves would manufacture and hopefully market soft contact lenses fabricated from Mr. Spriggs' buttons. One of these companies was Soft Lenses, Inc., of San Diego, Calif. They were the first.

The second one was the Milton Roy Co. in St. Petersburg, Fla. A third was Paris Optical in Coral Gables, Fla., and lastly was a company called FlexLens in Columbus, Ohio.

Soft Lenses, Inc., vigorously, and I mean vigorously, pursued an FDA approval of a soft contact lens made from Mr. Spriggs' material. After considerable testing, and after filing some 167 volumes of data and explanatory materials with the FDA, Soft Lenses, Inc., was granted the second FDA approval of a soft lens product in this country.

The relationship then between Soft Lenses, Inc., and Automated Optics was quite good. On the other hand, Soft Lenses, Inc., had to pay Automated Optics a 15-percent royalty. This was money out of their pocket and into Automated's. Nevertheless, the sales volume of Soft Lenses, Inc., increased dramatically. Except in March of 1977, and after having no inkling that this was happening, Soft Lenses, Inc., was granted a second FDA approval for a second Soft Lenses, Inc., contact lens, and apparently they were granted this approval in but 9 months with virtually no data.

Mr. GORE. Who was the contractor they entered into an agreement with for this second approval?

Mr. STEPNO. The contractor, or at least at the outset, the relationship was one between Burton-Parsons Co. of Washington and Soft Lenses, Inc., the two companies that you have noted in your opening statement.

And in fact, the basis for that agreement was a trade for a new plastic. This plastic was patented by Burton-Parsons. They made contact lens buttons out of it. They traded that to Mr. Brucker, the president of Soft Lenses, Inc., in exchange for a trademark in indeed the product "BoilnSoak," the preserved saline solution that was the subject of your first hearing.

Now, at the time all of us were just simply amazed that this approval, without the knowledge of anyone in the general public, could be granted so fast. At that time we requested through the Freedom of Information Act, whatever data and information we could get from the FDA on that approval. We got very little.

Mr. GORE. Let me briefly recap what you have said thus far, then I am going to ask you to proceed with your statement.

The soft contact lens industry for many years was dominated by Bausch & Lomb, which got the exclusive rights to the breakthrough in Czechoslovakia in the 1960's. They dominated the marketplace, got a big lead in the technology, and they in fact are still the leading company in this industry; is that correct?

Mr. STEPNO. Indeed.

Mr. GORE. They used the salt tablet solution, and in order to be approved by the FDA you have to get approval for the entire system; the lens, which is tested rigorously, and the fluid system to disinfect it and clean it and so forth.

Your company obtained approval of the second soft contact lens approved by the FDA in this country. The terms of your contractual agreement were the button fabricator, which took your raw material, the formula for which you invented—the terms of that contractual relationship were less than satisfactory to the other party, you believe they constituted a reasonable business agreement but, at any rate, they sought and established a second business relationship with the Burton-Parsons Co. The Burton-Parsons lens made in conjunction with the same contractor you had was approved in record time, sharply contrasting with the lengthy procedure you had to go through in order to get approval.

Burton-Parsons swapped the trademark, the patent on the new lens that it had, in return for the trademark and the formula to this preserved saline solution that Soft Lenses, Inc., had developed; is that correct?

Mr. STEPNO. Yes, that is essentially correct.

Mr. GORE. What we are going to do in this hearing is, we are going to examine in close detail the manner in which the Burton-Parsons application was handled at the FDA, whether in fact laws were violated in the process. And we are going to contrast the manner in which that application was handled with the manner in which your application was handled, and in fact the applications of all other companies in this field were handled, in order to see if once gain favoritism was shown in a way that bent the laws and regulations, if not blocked them, because of the close personal relationship between officials of that company and the two officials at FDA principally responsible for this area.

Is that a fair——

Mr. STEPNO. Yes.

Mr. GORE. I added something to your earlier presentation, but go ahead and proceed.

Mr. STEPNO. Mind you, at that time——

Mr. CORCORAN. One other thing I would like to get clarified in this swap that took place involving the patent, I don't understand how such a trade could take place before the patent was even granted, but you are an attorney, could you——

Mr. STEPNO. The patent was granted, I believe.

Mr. CORCORAN. It had been granted?

Mr. STEPNO. Yes, it had been granted, and also, this trade took place right in the middle of the proceeding whereby that second application of Soft Lenses, Inc., was being processed by the FDA.

Mr. CORCORAN. So you don't see any difficulty with that particular aspect of the history here?

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Mr. STEPNO. No, indeed. I have no trouble with Soft Lenses, Inc., having to pay a certain percentage of their net sales, in trying to switch to a different material. As a prudent businessman I would probably do the same thing. What does trouble me is how they did it.

Mind you, also at this time, of the four licensees, Mr. Spriggs, again, a small businessman, has all his production geared up to providing lenses for Soft Lenses, Inc.—buttons, excuse me. The other licensees who were also in the throes of trying to get their FDA approval on their particular lens, ordered much smaller quantities.

I am here today because in one particular magazine I saw the report on your first hearing and then contacted the staff to get a copy of that testimony, and that is where I saw the link between Burton-Parsons and Soft Lenses, Inc., and I see where apparently Burton-Parsons were able to get approval of an FDA laboratory without even inspection. They can get it over the phone. I believe there was testimony to that effect.

In light of that, I advised the staff that I had made an freedom of information request of the FDA, had received very limited material, and asked the staff whether they had anything from the FDA, also whether it would be possible to inquire of FDA to obtain any other materials that were submitted by Soft Lenses, Inc., themselves rather than the official data which was given to me?

I ultimately saw a paper styled, I believe, "Amendment to IND No. 7898." This paper was dated July 1975. I will backtrack a bit. IND–7898 was the IND file by Soft Lenses, Inc., on the Automated Optics material. The second material is not even remotely related to the first, namely, the Automated Optics material.

Mr. GORE. Let me again interrupt you to seek a clarification of exactly what you are saying here. I want you to correct me if I am wrong.

In order for a contact lens to be approved by the FDA, the material out of which the lens is made must be tested to make sure that when a human being puts it in his or her eye it is not going to cause some kind of health damage.

The approval process requires testing of the component itself. Burton-Parsons short-circuited that approval process by claiming that its lens was identical to or virtually indistinguishable from the lens that you had subsequently, had professionally collaborated with Soft Lenses on?

Mr. STEPNO. Not Burton-Parsons, Soft Lenses, Inc.

Mr. GORE. The application?

Mr. STEPNO. Was filed by Soft Lenses, Inc.

Mr. GORE. In both instances the application was filed by Soft Lenses, Inc.?

Mr. STEPNO. Exactly.

Mr. GORE. In the first instance, Soft Lenses filed an application that said, FDA, we have a lens that we have made out of materials supplied to us by Automated Optics?

Mr. STEPNO. Exactly.

Mr. GORE. You went through a lengthy testing procedure of the material you supplied to Automated Optics and FDA approved it.

Now, with the second lens, Soft Lenses, Inc., told FDA we want approval of this lens we have manufactured out of material suplied to us by Burton-Parsons. They had to receive approval for that second material to make sure it was safe and not harmful to human beings when they put it in their eye. In order to speed up that approval process, or to get around the requirement, Soft Lenses, Inc., told the FDA that the second material, supplied by Burton-Parsons, was indistinguishable from the first material that you supplied. Is that correct?

Mr. STEPNO. They went even farther than that; they said it was physically indistinguishable and chemically identical. They then made reference to the fact that at that time there was a lawsuit pending between Bausch & Lomb and National Patent and Automated Optics, and what their goal was was to establish an alternate source of manufacture.

Anyone reading that document filed in 1975 would believe that they were just simply seeking to get the Automated material made in another facility or make it themselves.

Mr. GORE. In your opinion, was this a false statement, a falsifying?

Mr. STEPNO. The statement "physically indistinguishable and chemically identical" is ludicrous from a chemical point of view.

Mr. GORE. Well, in order to establish the basis for further questions a little bit later on in this hearing, I would like to ask you to explain the differences between the material or the button that you supplied and the button that Burton and Parsons supplied, and we have a blackboard here if you would prefer to use the blackboard.

Mr. STEPNO. Yes, I would prefer to use the blackboard, Mr. Chairman.

Mr. Chairman, think of a polymer as simply paper clips stuck together, because essentially that is what it is, each one of the chips being a particular monomer or starting material from which the polymer is made.

Now I spoke earlier of the development in Czechoslovakia. The first generation lens, which is hema—you have seen this word come up in the other hearings. It is a hemabased polymer, all of these stuck together again in the paper clip chain.

Now in the first generation of patents issued to Professor Wichterle there was also disclosure of certain other materials that could be mixed with the hema to make a soft lens. And there was a minor amount of cross-linking agent—I am just going to put it here as an X. You have seen the word cross-linking agent. A polymer as such is not suitable for a lens because it would not be dimensionally stable. Every hundred units or so adjoining polymer chains are tied together with what is called a cross-linking agent. It doesn't really matter what the cross-link is so long as it is capable of tying the polymer chains together.

The second generation lens was the Seiderman lens. The Seiderman/Automated lens again had hema components, I will call it hema, but the characterizing feature is a rather exotic compound called N-vinylpyrrolidone. In particular in the commercial product, again there was also a cross-linking agent, it was roughly 80 percent hema and 20 percent NVP.

Now let's look at the second soft lenses' material, which was said to be physically indistinguishable; physically indistinguishable even though later on their big point was that it was three times stronger in tensile strength, a major physical characteristic; yet that is supposed to be indistinguishable.

Again, we have a hema base, but instead of Seiderman's N-vinylpyrrolidone, diacetone acrylamide was used. Diacetone acrylamide bears no chemical relationship to NVP. You can see that from the structure alone. And indeed, if you go back to the original Wichterle disclosure, one of the components that Professor Wichterle suggested as being compatible with his hema for a first generation lens was acrylamide.

And acrylamide is this; in diacetone acrylamide the only thing being added to the acrylamide is an innocuous tail. In effect it is a Wichterle lens. It is not at all related to the Seiderman NVP lens.

What then happened, after the paper styled "Amendment to IND–7898" was filed in July 1975, was a halfhearted attempt to obtain FDA approval, an attempt which included but 23 actual tests. Accordingly, the 1975 NDA was properly rejected, but in June 1976, yet another NDA was filed by Soft Lenses, again relying on IND–7898, which is not at all related to the product in issue.

Nine months later, this material was approved by Mary Bruch and Arnauld Scafidi, and lo and behold, another 9 months after that Mr. Spriggs goes to FDA, to the same people, Mary Bruch and Arnauld Scafidi, and says, Hi, we also have an improved material, it is even more improved than the tensile strength of the Soft Lens material, and he says, but we haven't done this, all we have done was, instead of 80–20, we are just changing proportions, we are making this 95 and we are making that 5.

The response from the FDA which was ridiculous, was that the Automated proposal required an entirely new IND. He could not even rely on the earlier IND–7898, on the same material in varying proportions, quote, if you change one ingredient one-thousandth of 1 percent, you have to start from scratch, Mr. Spriggs.

Yet with an entirely different material, certainly different by more than one-thousandth of 1 percent, soft lenses was accorded one particular treatment, they were even entitled to rely on Spriggs' own IND–7898, but Automated itself when proposing only a small change in proportions was told that Automated was not entitled to rely on such IND.

Where does Burton-Parsons now come into this? Burton-Parsons is the one developing the second material for Automated Optics, for Soft Lenses, excuse me. When the Seiderman material was developed, it was given the USAN or generic name, hefilcon.

Please bear in mind the statement in the first application that they were chemically indistinguishable and physically identical or something like that—what did they try to do to get a different generic name for the second material? Rather than hefilcon, they eventually added a "d" between the "e" and the "f" in hefilcon, styling it hedfilcon rather than hefilcon to add to the impression that that material was simply a me-too lens made by a different manufacturer. Even USAN would not accept that, it was so blatant—hey, find another name. Ultimately, that name was bufilcon.

Mr. GORE. Let me interpret you again to try to recap. I am trying to use this procedure because these chemical formulas are very, very complicated and complex. I personally am convinced that if the Congress is going to do a good job of oversight, in seeing that the FDA and other agencies are functioning properly, and not showing the kind of outrageous behavior that I think has occurred here and in the soft contact fluid case, then we are going to have to get down into the trenches and try to become a little conversant at least with some of these matters.

But basically, what you are saying is that the chemical structure of the material submitted to the FDA by Soft Lenses, Inc., which was supplied to them by Burton and Parsons, was very different, very different from the material that you had earlier supplied to Soft Lens, that was earlier approved by the FDA, yet the FDA accepted the assertion by Soft Lens that the two materials were identical, virtually indistinguishable?

Subsequently, you asked for approval of a third material that was very close in chemical structure, extremely close. You asked for the right to short-circuit that first step in the approval process by saying, Look, this is very close to the make-up of the first material we have already had approved, and they said No, it is absolutely impossible, you are going to have to go back to square one and start all over. So again you see a big difference in the way Burton and Parsons is treated by these people at FDA and the way you were treated.

How about the requirements for human testing for your material as opposed to the Burton-Parsons material?

Mr. STEPNO. Again, when you said similar material, the Automated second material versus the Automated first material, they were not similar chemically, they were identical. The only thing that was changed was the relative proportions of ingredients, but, other than that, the polymer was chemically identical. And again, to temper your thoughts too, there were also three other licensees out there seeking FDA approval with precisely the identical material as the Automated one material, namely, it was the same chemically and it was in the same proportions.

Mr. GORE. They were also denied the right to do that?

Mr. STEPNO. Well, ultimately they did receive approval.

Mr. GORE. But not——

Mr. STEPNO. Time was important.

Mr. GORE. How many human subjects did you perform tests on to receive your approval from FDA?

Mr. STEPNO. Well, again Automated does not make contact lenses.

Mr. GORE. How many human subjects were tested by Soft Lens to get approval of your material?

Mr. SPRIGGS. 3,755 lenses.

Mr. STEPNO. 3,755 lenses were used in the studies.

Mr. GORE. How many tests were performed by Soft Lenses to get approval of Burton and Parsons material?

Mr. STEPNO. I am not really sure. I am not sure that that is clear from the record.

Mr. GORE. We will show in later testimony that there may have been none, that it is questionable that any were done, but that if any were done there were a very few.

We are going to adjourn for 5 minutes or maybe 6 minutes, but no longer than that because we have a vote on the floor. We are going to recess for 6 minutes.

[Recess.]

Mr. GORE. The subcommittee will come back to order.

The last question I asked was about the human studies.

When you developed the new version of your material and you had the meeting with FDA about getting it approved, you requested the opportunity to do as Burton and Parsons and done?

Mr. STEPNO. As Soft Lenses had done.

Mr. GORE. How many human studies would you have had to conduct in order to get approval on your new material?

Mr. STEPNO. Even more than that—the full route of IND, NDA, and all amendments, was suggested by the FDA. No referrals to the earlier IND were to be permitted. The comment was made, Automated has "changed one ingredient one-thousandth of 1 percent" and must go the full route. Then the numbers first suggested by FDA were "from 800 to 1,200 human studies." After a lapse of several minutes, it was then suggested that "perhaps you could get by with 500." An upshot of all that was that it was simply not economically viable to go the full route on this new material at that particular time.

Mr. GORE. I would like, without objection, to put into the record a chronology of all these events. [See p. 38]

I think this chronology will show where at one point you used the month of July, I think it was June instead. Let's clarify the length of time we are talking about.

You have been using the figure 9½ months. The total amount of time for the approval of the Soft Lenses product, using your testimony, was longer than that, right?

Mr. STEPNO. Considerably longer.

Mr. SPRIGGS. The research was started in September 1970.

Mr. STEPNO. Approval was granted in April 1974, entailing some 167 volumes of material submitted to the FDA.

Mr. GORE. Well now, the length of time that it took Soft Lenses to get approval for the Burton-Parsons material was also longer than 9 months total, wasn't it? It took longer than that all together?

Mr. STEPNO. That's open for debate. If you consider the June 13, 1975, submission of "Amendment to IND, 7898," and extrapolating that against the March 1977 date, we are talking about some 20 months. However, in that time period, June 13, 1975, to the resubmission of the second Soft Lenses NDA, in I believe June 1976, and consider what actually was done in that period, I am not so sure that the 9 months is not the more valid date.

Mr. GORE. That is fine. We will ask you to stay in the hearing room, if you can. We may have further questions for you later.

Does counsel for minority have questions?

Mr. STEWART. No.

Mr. STEPNO. When the Seiderman material was developed and advertised by Soft Lenses, Inc., in their early advertising, their

trademark was simply PHP and the Seiderman lens became known as the PHP lens. I am looking at the summary basis for approval we received, and it says Hydrocurve II Lens, PHP. Now, how PHP ever got in there I don't know. This is from the Freedom of Information material we received.

The further statement about the polymer is consistent. It is not consistent with any structure on the blackboard [indicting]. Again, the Automated lens, the trademark for that was Hydrocurve. In switching to this new material, while maintaining the trademark of Automated Optics, Soft Lenses simply called the product Hydrocurve II, which was supposed to be "physically identical."

Mr. GORE. So they presented this new lens to the public as identical to the earlier lens, just as they presented it to the FDA as identical to the earlier lens. Of course, the public has no way of knowing that it is a completely different product, because the FDA had certified it as being identical.

Mr. STEPNO. They even attempted to get the generic name "Hedfilcon," and that is why I am a confused lawyer this morning.

Mr. GORE. Thank you.

We would like for you to stay around and we will discuss some of the matters we discuss with our next panel.

Our next witness is Hon. Jere Goyan.

If you remain standing and raise your right hand.

[Witnesses sworn.]

Mr. GORE. I would note for the record that Dr. Goyan is also accompanied by Nancy Buc, chief counsel.

Welcome. Please proceed with your presentation.

TESTIMONY OF JERE GOYAN, COMMISSIONER, FOOD AND DRUG ADMINISTRATION, PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH AND HUMAN SERVICES, ACCOMPANIED BY J. RICHARD CROUT, M.D., DIRECTOR, BUREAU OF DRUGS; MERLE GIBSON, M.D., DIRECTOR, DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS; NANCY L. BUC, CHIEF COUNSEL; AND WILLIAM KOCHET, CHEMIST

Mr. GOYAN. Thank you very much.

I am here today at the subcommittee's invitation to discuss the FDA's regulation for soft contact lenses, and in particular the approval process for the applications submitted in the 1970's by Soft Lenses, Inc. I would like to deliver a brief, prepared statement and then answer any questions that you may have.

The subject of the effect of DA's regulatory activities on the regulated industry is certainly not a new one. For more than a decade there have been frequent allegations and debates concerning the new drug application—NDA—process as a barrier to the marketing of the new drug entities.

Among other issues, one recent focus of interest has been the soft contact lens and how FDA's regulation of it has affected the public and the industry. Today I would like to place the history of soft contact lenses in the perspective of other newly developed drug products, even though soft lenses are now regulated as devices.

The soft lens is a product that was first marketed in this country almost a decade ago. Although it was not the type of new chemical entity that the Bureau of Drugs was accustomed to regulating, it

was regarded as a drug because of its interaction with the eye and its capacity for absorbing chemicals and transferring them to the eye. Because soft lenses were not typical drug products and because they were manufactured by an industry that was largely unfamiliar with FDA regulation, special problems were posed in incorporating soft lenses into the new drug review process. Both FDA and the industry had a great deal of learning to do about each other and about the lenses themselves and their accessories.

In addition to the scientific and regulatory problems associated with our coming to grips with the emerging technology of soft lenses, the work of FDA was further complicated by the passage of the Device Amendments to the Federal Food, Drug, and Cosmetic Act. These provisions became effective May 28, 1976, and required a transfer of responsibility for soft contact lenses and their accessories from the Bureau of Drugs to the Bureau of Medical Devices. That transition took place in two stages. The first occurred on May 28, 1976. After that date, soft lenses continued to be reviewed by the Bureau of Drugs' staff, but they were subsequently submitted to review by a Bureau of Medical Devices Advisory Committee before being approved by the Director of that Bureau.

The second stage of the transition was the complete transfer of applications, reviews and authority for approval to the Bureau of Medical Devices on October 31, 1978. Viewed in this context of change, I believe the record of submissions, reviews and approvals is a rather good one, and I believe the Bureaus deserve credit for effecting a smooth transition under difficult circumstances.

Currently some 30 contact lens applications have been approved for marketing. One element in the NDA review process that I believe aided FDA and the industry in the learning process was our early and consistent development and use of guidelines. Detailed guidelines were developed in conjunction with an Ophthalmic Drugs Advisory Committee during 1971–72.

FDA recognized that the soft contact manufacturers were almost totally unfamiliar with drug clearance procedures and held a workshop in September 1972 to which all manufacturers were invited. The participants reviewed in detail these guidelines. Guidelines were in effect for clinical trials, manufacturing, microbiology, and pharmacology. These guidelines have been revised over the last 10 years to keep pace with this developing technology. The latest revision was made available by the Bureau of Medical Devices in June of this year.

I might add that guidelines are especially helpful in protecting the agency from the necessity of relying solely upon the judgment of individual reviewers. Although we must always depend upon the expertise of our reviewers, we recognize our obligation to assure that, to the greatest extent possible, all applications were reviewed using the same ground rules.

In reviewing the history of approvals of applications, it is always important to recognize that in our process no one individual controls the speed or outcome of reviews of NDA's. Diverse elements of the agency are called into play to review the medical, pharmacologic, chemical, and microbiological aspects of the application, as well as the manufacturing of the product at the site. This institutional approach insures input by experts in each relevant area and

does, I believe, minimize the opportunity for inappropriate influence by the industry or other affected parties in the decisionmaking procedures.

Since the subcommittee specifically asked about the new drug approval process for two lenses from Soft Lenses, Inc., San Diego, Calif., which carry the trade names of Hydrocurve I and Hydrocurve II, I would like to outline briefly the history of the approval process for these two lenses. The investigational new drug exemption—IND—for Hydrocurve I, which was a lens made from a modified and crosslinked hydroxyethyl monomethacrylate—HEMA—polymer was submitted to the agency on May 12, 1971. The NDA for this product was submitted about a year late, June 26, 1972. The lens material for the product was supplied by Automated Optics, Inc., Englewood, Colo.

There was a series of correspondence between FDA and the firm regarding deficiencies in the application. Further complicating the review of this application was the fact that the responsibility of the review of soft contact lenses was transferred in January 1974 within the Bureau of Drugs from the Division of Surgical and Dental Drug Products to the Division of Anti-Infective Drug Products. The application for Hydrocurve I was finally approved on April 30, 1974, 22 months after the original submission.

The application was approved with instructions calling for cleaning the lenses with Boil 'n Soak, a solution manufactured for Soft Lenses, Inc., by Burton-Parsons; Pliagel, a solution from Flow Pharmaceuticals, or a Barnes/Hines soft lens cleaner. After the lens was approved, Soft Lenses, Inc., apparently became concerned over patent suits against Automated Optics and so they looked for a similar polymer they could use in their lenses. They selected one made by Burton-Parsons and performed a small clinical study with 23 patients using that lens. The record is unclear, but the study appears to have been performed without notification of FDA until June 13, 1975, when Soft Lenses, Inc., submitted an amendment to the Hydrocurve I IND.

On July 11 of that same year, an NDA was submitted for the revised Hydrocurve I lens which was to become known as Hydrocurve II. In February 1976 the firm was notified that the application was not approvable because additional clinical trials were required. In June 1976 the firm resubmitted the application with a new series of clinical studies, as well as information that Soft Lenses, Inc., was now beginning to manufacture the lenses themselves from their own raw materials.

It appears that these clinical studies were performed using the Burton-Parsons lenses. However, the Soft Lenses, Inc., lenses were made to be identical to the Burton-Parsons polymer, according to data supplied by the firm. After an exchange of correspondence and some further work, the NDA was finally approved on March 31, 1977. This approval took a little over 20 months from the original submission. The Hydrocurve II lens provided for both hot and cold disinfection systems supplied by Burton-Parsons.

Mr. GORE. You are measuring these time periods from the beginning of the NDA, not from the beginning of the IND?

Mr. GOYAN. That is correct. It is impossible to measure those, because the process is under the control of the company.

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Mr. GORE. It is partially under the control of both. If the IND is short circuited for one reason or another by FDA, then that time period is relevant, is it not?

Mr. GOYAN. I would assume the driving force is what the FDA requirements are.

Mr. GORE. They can't start the human tests before the IND is approved?

Mr. GOYAN. That is right.

Mr. GORE. So the relevant time period is from the beginning of the process to the end of the process, not from the beginning of the NDA.

Mr. GOYAN. That wouldn't be true. In every case it differs.

Mr. GORE. If a company is to get approval from FDA, it has to start with an IND. If we are to compare company A with company Z, then it makes sense to look at how long it has taken from square one all the way through the process, rather than eliminating the IND procedure from that comparison.

Mr. GOYAN. I am not sure I agree with you on that comparison.

Mr. GORE. If there has been an arbitrary decision, or a decision based on other than scientific judgment, not to require an IND, then that time period is indeed relevant.

Mr. GOYAN. I agree with that entirely.

Mr. GORE. What you are comparing in these is after the IND step has taken place?

Mr. GOYAN. That is correct.

Mr. GORE. Go ahead.

Mr. GOYAN. The FDA has learned a number of lessons which are helping us improve this review and approval process and I believe that we will continue to do so, whenever new and innovative product applications are submitted to the Agency. The basic philosophy underlining many of our decisions in regulating these products is that when dealing with what is essentially a cosmetic product, or one that is not a medical necessity, we must be especially watchful for hidden dangers and the potential for injury.

This is especially true of products for use in and around the eye, where the consequences of product misuse are so serious. The history of the salt tablet disinfection systems makes the point fairly well, I think. Reviewers in the Agency believed then, and still believe, that salt tablets, which were then used to make up unpreserved solutions for disinfecting the soft lens, carried substantial risks, especially when they were improperly handled. How those risks were evaluated, and how the benefits were weighed is always subject to reevaluation in hindsight, but a prudent course of action was followed in this case.

The Agency certainly has been sensitive to, and sympathetic with, consumer needs for better and less expensive ways of cleaning and disinfecting soft contact lenses. It is not the role of FDA to initiate product development or to become involved in commercial considerations. However, we have worked with industry to overcome some of our concerns with the salt tablets. In fact, in July we approved a modified salt tablet which has a boilable mixing bottle and very detailed user and practitioner instructions.

We believe these changes have provided for a much safer product for contact lens disinfection than was the originally approved salt

tablet. In addition, FDA approved in August 1979, and subsequently, three unit-dose nonpreserved saline solutions, which should alleviate the problem of reactions to preservatives experienced by some individuals.

I believe that this history demonstrates a responsive and responsible attitude on the part of the Agency in balancing the desires of the consumer for their soft lenses and, at the same time, protecting the public from potential hazards associated with these products.

That concludes my prepared statement. My colleagues and I will be glad to answer any questions you may have.

Mr. GORE. Thank you, Dr. Goyan.

Before going to the alleged favoritism in the approval of this new contact lens which Burton and Parsons participated in, I would like to follow up with you the actions of the FDA subsequent to this subcommittee's last hearing on the disinfectant fluid.

We found in our last hearing—as I said in my opening statement, we found that the cheap salt tablets were declared unsafe and that one of the reasons for this was 200 alleged cases of health problems caused by salt problems which were reported to an FDA funded national registry by an FDA medical officer. Do you believe that those 200 cases of alleged adversary actions are real?

Mr. GOYAN. I am not sure whenever they are real or not. I don't think they are scientifically justifiable.

Mr. GORE. Have you had an opportunity to review the record of our last hearing?

Mr. GOYAN. Yes, I have.

Mr. GORE. Do you think it possible that Dr. Scafidi actually received muffled telephone calls from anonymous doctors afraid to give their names, then sat down and changed the color of them in every few entries and then compiled a notebook with none of the supporting data required for such entries? Do you believe that is plausible testimony?

Mr. GOYAN. I am not sure whether it is plausible. I think it is possible. I do believe that matter is before the Inspector General, and I anticipate receiving a report from her, hopefully at an early date.

Mr. GORE. We have become a little impatient with the Inspector General over there. The Federal Bureau of Investigation is now working on it also, and the Attorney General in Baltimore is also investigating this matter. But you have a responsibility as the head of the FDA to clarify any information that is put out by the FDA upon which the industry and the public relies. And these 200 cases of alleged adverse reactions to salt tablets are still out there in the public domain. It is used in advertising. You may have seen the television commercials that claim salt tablets are unsafe.

[Testimony resumes on p. 32.]

[The following material was submitted for the record:]

CONGRESS OF THE UNITED STATES
HOUSE OF REPRESENTATIVES
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS
OF THE
COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE
WASHINGTON, D.C. 20515

ROOM 2323
RAYBURN HOUSE OFFICE BUILDING
PHONE (202) 225-4441

MARK J. RAABE
CHIEF COUNSEL/STAFF DIRECTOR

September 10, 1980

Honorable Jere Goyan
Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Mr. Commissioner:

Reference is made to your letter of August 22, 1980, outlining certain steps you have taken following the Subcommittee's hearing into the FDA's removal from the market of salt tablets for use in connection with soft contact lenses. There is an additional, highly important matter which you apparently have not addressed.

As you know, serious questions were raised during the hearing about the legitimacy of Dr. Scafidi's notebook. Moreover, there is apparent agreement over its deficiency as scientific data, as indicated in the following colloquy:

Mr. Gore: Would you consider the entries in this notebook as scientifically admissible data?

Dr. Crout: No. I have seen a xerox of this before and asked myself that question. The answer is no. [Transcript at page 125]

Later in the hearing, Congressman Gore noted that an article about the National Registry appearing in the February 1980 issue of the Journal of the American Academy of Ophthalmology contained the questionable information from the Scafidi notebook. Mr. Gore expressed the concern that this information would be disseminated to ophthalmologists all over the country under the apparent imprimatur of the FDA. Dr. Crout responded, in part, that "(a)s soon as this hearing is over I will go back and see how that survey reports out information. I would agree that report does not have a high degree of scientific credibility." [Transcript at page 127]

It has now come to my attention that subsequent to the Subcommittee's hearing, Bausch and Lomb has distributed promotional materials dated July 7, 1980, which indirectly cite Dr. Scafidi's data by reference to more than 200 cases of corneal infections contained on the National Registry. In this instance, the Scafidi data is being used to disparage the use of salt tablets, which, as you know, have now been approved by FDA for use under certain circumstances.

In view of the highly questionable nature of the Scafidi data on the National Registry, and the use of that data for scientific, competitive or promotional purposes, I believe it is imperative that you take appropriate and prompt action to purge that information from the Registry. In this connection, I would remind you that the Registry grew out of an FDA-funded project. Moreover, since the Scafidi data has been widely disseminated, it has become necessary to give equally wide publicity to any FDA action removing that data from the Registry.

I look forward to hearing the details of the action you will take in this regard. Your prompt attention and cooperation will be appreciated.

Sincerely,

Bob Eckhardt

Bob Eckhardt
Chairman
Subcommittee on
Oversight and Investigations

cc: Honorable Albert Gore, Jr.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

NOV 21 1980

Honorable Bob Eckhardt
Chairman, Subcommittee on
Oversight and Investigations
Committee on Interstate and
Foreign Commerce
House of Representatives
Washington, D. C. 20515

Dear Mr. Eckhardt:

This letter responds further to your letter of September 10, 1980, about information in the National Registry of Ocular Drug Induced Adverse Effects on eye problems in users of salt tablets for disinfection of soft contact lenses.

Because the salt tablet information has been publicized and used in a national advertising campaign, we agree that public correction of the information available to physicians is necessary and that we should assure that this information is not further used in the Registry. To that end, we have asked the director of the Registry to publish in a national ophthalmological journal a discussion of the limitations on interpreting adverse reactions data, with specific reference to salt tablets and solutions. He has agreed to do this, and we shall send you a copy when it is published.

We share your concern that the registry contain data of high scientific credibility; we would like to outline the steps we are taking toward insuring this goal.

The extramural grants and contracts program of the Bureau of Drugs' Drug Experience and Trends Analysis project are scheduled to be reviewed this year by a panel of outside advisors and Bureau staff. This project includes various registries, including the Registry of Ocular Drug Induced Adverse Effects.

Some problems are common to all registries of this type. It is desirable that a registry serve as an early warning mechanism and signal potential problems with drugs. The earliest reports are made by physicians who suspect an association between a drug and an adverse event. Early reports may signal the existence of a problem, but are rarely sufficient to permit drawing firm conclusions of association. The incidence of the event in patients not receiving the drug, the prominence of the event, the temporal relationships between the drug therapy and the event, and the biological plausibility of the association are factors which must be considered in the determination of the likelihood that the drug caused the event.

Early reports from physicians are highly desirable as an alert and we encourage them, but they must be interpreted cautiously until more reports and more information from other sources accumulate. A registry should try to make an evaluation of the likelihood that a reported event is drug induced; algorithms for this purpose are being incorporated into the registries. The director of the eye registry recently spent some time with the Bureau of Drugs' staff for an orientation that included the purposes and need for using an algorithm to assess the likelihood of causation. The algorithm used by the Division of Drug Experience is found on page 10 of the enclosure.

Because reports to registries are sent in by a variety of parties--e.g., practicing physicians, research physicians, drug firms, and consumers--their quality varies considerably. Some reports contain extensive information and the possible relationship of the event to the drugs can be appraised readily. Other reports are sketchy and do not contain sufficient information on the factors necessary to evaluate probable causation accurately. The weights given to these two types of reports should be very different, although both may be useful in specific circumstances.

The information on salt tablets is mainly of the second type. The reports are not sufficiently detailed to show that serious eye infections are more common with salt tablets than with other methods of disinfection; no good comparative information is available. It is reasonable to suspect that salt tablets may carry such a risk, but the information is not definitive on the point.

I certainly share your desire that FDA decisions be based on solid scientific data. If I can provide any additional information on this issue, please let me know.

Sincerely yours,

Mark Novitch, M.D.
Acting Commissioner of Food and Drugs

Enclosure

This is the transcript of the TV ad run by BL in July and August 1980;

The speaker in the ad says the following:

"I've got the soft life. Soft contaet lenses and easy lens care with pre-mixed BL [illegible] saline solution. Remember-do-it-yourself salt tablets and distilled water? Forget them. B&L preserved saline solution is faster because it's pre-mixed, safer because it's sterile, and buffered, so it's easy on your eyes. B&L saline solution. It's a lot more than just salt and water. Come over to the soft life. Soft lenses and lens care products from the leader in soft lens science, B&L. "

BAUSCH & LOMB

SOFTENS DIVISION · OPTICAL CENTER · 1400 NORTH GOODMAN STREET · ROCHESTER, NEW YORK 14602 · (716) 338-6000

June 23, 1980

Dear Pharmacist:

Since November, 1978 when Bausch & Lomb discontinued the domestic shipment of salt tablets, a few brands of salt tablets have remained on the market. We want to alert you to the potential risks you face for dispensing, to soft contact lens wearers, salt tablets unapproved for preparation of saline solution to be used with soft contact lenses, or in preparing normal saline for this purpose.

1. Since no government approval now exists for the brands of salt tablets currently available for use with soft contact lenses, responsibility for any adverse consequences may lie with the dispenser as well as the manufacturer.

2. Since no instructions for use with soft contact lenses or warnings against such use are given with the tablets, any misuse of the product by a soft contact lens wearer leading to complications caused by a failure to provide such instructions may be the dispenser's responsibility.

3. If you are currently dispensing salt tablets to soft contact lens wearers you may wish to check with your malpractice insurance carrier to determine if the carrier covers adverse consequences resulting from use of a product for unapproved indications. You should also check with your carrier to see if you are personally liable, should an adverse reaction, such as loss of an eye, occur, and if so, does your carrier provide you with coverage for this.

Serious eye problems have been reported* as a result of patient non-compliance with mixing and use of a soft contact lens solution prepared with salt tablets and distilled water.

Since approved, safe and convenient alternatives such as Sterile, Preserved Saline Solution and Sterile Saline Solution (preservative-free, unit dose) are available from several manufacturers, we urge you to consider the risks involved with continued recommendation of currently available salt tablets to soft contact lens wearers.

Sincerely,

C. O. Titus

*Information available upon request

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BAUSCH & LOMB
SOFLENS DIVISION

news

FOR RELEASE: IMMEDIATE

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SALT TABLET REGIMEN MAY POSE PATIENT RISK, STUDY SHOWS

Almost eight out of ten patients who use salt tablets for the disinfection of soft contact lenses do not mix fresh solution daily according to a recent family-population study conducted by National Family Opinion, Inc.

Only two out of ten patients interviewed said they mix fresh solution daily. Furthermore, the study shows a low frequency rate for disinfection. Only 48% of salt tablet users claimed they disinfected their lenses daily.

These findings confirm the validity of the various objections to salt tablet regimens which were previously cited by the Food and Drug Administration in requesting withdrawal of the product from the market. "These limitations," according to the FDA, "included possible bacterial contamination and improper solution preparation."

One cardinal rule in developing medical devices or systems for patient use is to design the system to be as safe as possible. A

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--more--

salt tablet regimen, however, may not meet this standard. Its multiple components are subject to hazards beyond the practitioners' control such as: patient non-compliance, water contamination, and mis-mixing.

Patient compliance is key to the efficacy of a system that requires that patients follow all procedures exactly when they mix their own disinfecting solutions. When patients do not prepare fresh saline daily, the risk of microbial growth is magnified because patient-prepared saline solutions contain no preservative. The longer the interval between preparation of fresh-saline, the more likely it is for the solution to become contaminated.

It has been a common assumption that only a small number of patients will fail to comply with recommended procedures. The National Family Opinion study, however, reveals that 77% of the salt tablet users surveyed do not mix fresh solutions daily. 89% of those who do not mix fresh solution daily indicate that their unpreserved saline solution is kept for two or more days before fresh solution is mixed.

With daily disinfection of soft contact lenses a key to effectiveness of salt tablet regimens, lack of patient compliance presents the risk of infection. Recently, the National Registry of Drug-Induced Ocular Side Effects reported that more than 200 cases of corneal infections were seen in patients using salt tablets. In most cases the bacteria cultured from these infections were Staphylococcus aureus; others indicated Pseudomonas aeruginosa, streptococcus species and fungi. According to the Registry, "the product (salt tablets)...suffered because there was no preservative."*

*"Interim Report: National Registry of Possible Drug-Induced Ocular Side Effects", presented at the 84th Annual Meeting of the American Academy of Ophthalmology, Nov. 1979.

The cases reported by the Registry, however, may represent only the tip of the iceberg, according to Carl Kupfer, M.D. of the National Eye Institute. In a discussion of the Registry's Report, Dr. Kupfer notes: "There is every reason to believe that ophthalmologists do not routinely report all untoward drug side effects...the incidence of adverse effects probably represents a low estimate, but one cannot determine precisely by how much the incidence is unreported." The high incidence of non-compliance reported by the National Family Opinion survey would indicate that Dr. Kupfer may indeed be correct in his assumptions.

The need for patient compliance is inextricably tied to problems with distilled water required to be used in conjunction with the salt tablet for saline solution preparation. The purity of distilled water is generally taken for granted by both practitioners and patients alike. The assumption is often false.

Dr. Donald Ahern, professor of microbiology at Georgia State University, has stated it is apparent that use of distilled water may be risky. Most of the bottles of distilled water samples he has examined contained relatively few microorganisms when first opened. But once in a bathroom for a 24 to 48 hour period, the containers had relatively high concentrations of organisms. Dr. Ahern explained that two out of eight new gallon jugs in his sample contained Pseudomonas aeruginosa. After the containers were in use -- a maximum of three days in Dr. Ahern's study -- each container was contaminated.

Louis Wilson, M.D., of Emory University conducted tests of distilled water with similar results. Dr. Wilson indicated that contamination of distilled water occurs over a short period of time after the container is opened. Furthermore, gram negative organisms having simple metabolic requirements can replicate in solutions like distilled water and saline.

The problem of distilled water contamination illustrates the importance of daily disinfection of soft contact lenses by patients following salt tablet regimens. All practitioners, particularly those whose patients still use salt tablets, should therefore be mindful of the patient risk posed by lack of compliance with the disinfecting regimen.

Findings of Study to Measure Compliance of Salt Tablet Users Conducted by National Family Opinion, Inc., New York, N.Y.

For this study, 20,000 families were contacted originally and almost 900 soft contact lens wearers were identified. These received a second questionnaire asking for more detailed information. Eventually 183 individuals were identified as salt tablet users. During the first week of February, 1980, an attempt was made to contact all by telephone for an interview. One hundred salt tablet users were interviewed. These were the findings:

Q2 -- How frequently do you mix fresh saline solution?

every day	23	(23%)
every other day	15	(15%)
every 3 days	16	(16%)
every 4 days	5	(5%)
every 5 days	7	(7%)
less than once every 5 days	34	(34%)
	100	

Q3 -- Once you've mixed a bottle of saline solution, how many days do you keep it before mixing saline solution again? (Asked of those who don't mix every day.)

less than 1 day	1	(2%)
1 day	7	(9%)
2 days	11	(14%)
3 days	16	(21%)
4 days	4	(5%)
5 days	8	(10%)
over 5 days	30	(39%)
	77	

Q4 -- How frequently do you disinfect your lenses?

every day	48	(48%)
every other day	10	(10%)
every 3 days	6	(6%)
every 4 days	2	(2%)
every 5 days	6	(6%)
less than once every 5 days	28	(28%)
	100	

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July 22, 1980

Jere E. Goyan, Ph.D.
Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Re: Blairex Laboratories, Inc.
Salt Tablets for Use in Heat Disinfection of Soft Contact Lenses

Dear Commissioner Goyan:

Please refer to my previous letter, dated July 1, 1980, to which you have not replied to date. An additional development has taken place concerning the above matter. This latest development further prejudices our clients as a result of your agency's actions.

My information is that the enclosed materials have been distributed nationally to pharmacists (Enclosure 1) and to editors of the professional press (Enclosure 2) by Bausch and Lomb. These materials represent an attempt by Bausch and Lomb to convince pharmacists and other health professionals (and, through them, the general public) that there are serious and significant dangers associated with the use of salt tablets for the heat disinfection of soft contact lenses. Such representations are completely unfounded, false, and misleading.

In support of its allegations, the Bausch and Lomb material relies heavily on two factors:

1. "[N]o government approval now exists for the brands of salt tablets currently available for use with soft contact lenses." (See Enclosure 1)

2. "Recently, the National Registry of Drug Induced Ocular Side Effects reported that more than 200 cases of corneal infections were seen in patients using salt tablets." (See Enclosure 2, page 2)

Neither of the above factors constitutes a legitimate reflection of the safety of salt tablets. They do, however, reflect on the Food and Drug Administration's failure to protect the public interest in this matter.

Lack of Government Approval

The fact that salt tablets have not yet reappeared in the marketplace specifically labeled for use with soft lenses does not reflect adversely on the well-established safety of this product. It is, rather, the result of unjustified and inexplicable bureaucratic delay and indifference, both to the merits of the case and to the fate of a small manufacturer. Our client has waged an uphill battle since last year to reverse the FDA's completely unjustified removal of salt tablets from the market. Our client's effort has, moreover, been very much in the public interest. Recent Congressional hearings have confirmed the results of our own inquiries: the withdrawal of salt tablets was a completely unjustified regulatory action which has needlessly cost American consumers hundreds of millions of dollars.

As a result of prolonged and detailed discussions with the staff of the Bureau of Medical Devices, Blairex Laboratories submitted a Premarket Approval Application for a redesigned and relabeled salt tablet product. The application was approved by the Ophthalmic Advisory Panel on June 2, 1980. In our previous discussions with Bureau staff, we were advised that a letter of approval would be released to us very quickly after the panel's approval of our application. Initially, the Bureau staff estimated that the approval letter would be released some time during the week following the panel's meeting. This original estimate was then lengthened and, as of last week (six weeks after the approval of our application by the advisory panel), the Acting Director of the Bureau has declined to provide any estimate of when this approval letter might be released.

At a public hearing, on July 1, 1980, there was a gratuitous and illegal partial disclosure of the content of our pending application by an FDA official. I called this to your attention in my letter of the same date. Even this highly prejudicial -- and unprecedented -- event has failed to produce any compensating expedition of our client's approval letter. Such expedition was obviously called for, in the interest of fair play, to mitigate the competitive injury done to our client by this disclosure.

In Section 515(d)(1)(A) of the Act, Congress has provided that action on applications for premarket approval shall be

taken "as promptly as possible." This statutory standard has not been met in this case.

The unjustified withholding of formal approval, as the enclosed material should demonstrate to you, has now afforded Bausch and Lomb an opportunity to pursue its own competitive objectives by means of a mailing asserting, in effect, that the salt tablet (which that same company continues to sell in Canada) is a dangerous product, the use of which exposes a practitioner to malpractice liability.

Adverse Reaction Reports at the National Registry

The other factor upon which the Bausch and Lomb mailing chiefly relies for its plausability is the alleged information in the possession of the National Registry documenting approximately 200 instances of corneal injury due to misuse of salt tablets.

As you well know, at a recent hearing of the Oversight and Investigations Subcommittee of the House Commerce Committee (July 1, 1980) it was alleged (with supporting evidence) that this information -- which was supplied in undocumented fashion by an FDA employee by means of a tape recording -- is highly suspect and may have been fabricated to rationalize the agency's previous action in removing salt tablets from the market. Such allegations aside, the report on its face constitutes unverified hearsay twice removed. At the Oversight and Investigations Subcommittee hearing Dr. Crout said that this material is not "scientifically useful." He also expressed his disapproval of an interim report, referring to this unverified material, published by the Director of the Registry. Yet, this same interim report is now referred to by Bausch and Lomb in its press release of July 7 (see Enclosure 2, page 2) as evidence of injuries due to salt tablets.

The Bausch and Lomb material also refers to a study by National Family Opinion, Inc. The portion of the study referred to by Bausch and Lomb alleging failure by consumers to properly sterilize their soft lenses would (if it is an accurate summary of the study considered as a whole) represent noncompliance with the directions for use of the soft lenses themselves and the related disinfecting units. Yet Bausch and Lomb presents this as evidence of noncompliance with directions for use of salt tablets. Furthermore, the study is silent as to the use of unpreserved saline as an eyedrop -- the alleged misuse cited by Bureau Staff. Mere retention of unpreserved saline does not of itself result in adverse consequences. I also note that this National

Family Opinion material was supplied to the Ophthalmic Advisory Panel at its meeting on February 11, 1980; it is not new.

As to the Bausch and Lomb company's statement that "use of distilled water may be risky," (Enclosure 2, page 3) I note that the SOFLENS® Enzymatic Contact Lens Cleaner, like the salt tablet, contains no preservatives. The SOFLENS® product, like the salt tablet is dissolved in distilled water. I suggest that the company's expressed apprehensions on this point be evaluated against that background.

Conclusion

In light of the above factors, I respectfully request that you take the following immediate actions to protect our client's rights and the public interest:

1. Direct the Bureau of Medical Devices to immediately release the letter of approval for our Premarket Application. Failure to do so only prolongs what has already been a regrettable regulatory episode. The failure to release this letter also delays the availability of specifically labeled salt tablets incorporating the detailed labeling directions and warnings which your staff has repeatedly stated are essential to the safe and effective use of salt tablets. Consumers, until such a product becomes available, will -- as you know -- continue to make use of the generically labeled salt tablets which contain no such instructions or warnings.

2. Withdraw the report provided to the National Registry until its probity and authenticity have been verified by an impartial source. At present, the continued status of this highly suspect material as a purportedly official report of the FDA is being misused, for competitive reasons, in a campaign to create unjustified apprehension and fear on the part of the public and health professionals.

I hereby reiterate my request for a meeting with you on this subject. Our client, admittedly, is a small company. But I nevertheless suggest that the issues involved here, and the magnitude of the expense being imposed on the public, fully justify your personal concern and attention. I look forward to your response.

Sincerely,

Daniel J. Manelli

DM:apb
Enclosures

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August 18, 1980

Nancy L. Buc, Esquire
Chief Counsel
Food and Drug Administration
5600 Fishers Lane
Room 657
Rockville, MD 20857

Dear Ms. Buc:

Thank you for your letter of August 11, 1980, responding to my letters of July 1 and July 22, 1980.

In my letter of July 1, I objected to a portion of Dr. Crout's prepared testimony at a hearing before the Sub-committee on Oversight and Investigations, House Commerce Committee. I agree that the subsequent approval, on July 31, 1980, of our client's premarket approval application has obviated the need to pursue that matter further.

Your letter does not, however, respond to another issue, which I raised in my letter of July 22, 1980. In that letter I called the Commissioner's attention to recent communications to pharmacists and the trade press by Bausch and Lomb, Inc. These mailings, inter alia, disparaged the safety of salt tablets and asserted that the National Registry of Drug-Induced Ocular Side Effects has documented approximately 200 cases of corneal injury secondary to salt tablets. The source of these reports, as I pointed out in my letter of July 22, was an FDA employee.

I detailed in my July 22 letter my reasons for requesting that the Commissioner withdraw this report from the National Registry until its validity can be independently established. This issue has not been rendered moot by the approval of our client's application. I would, therefore, appreciate your addressing this issue and advising me as to what action the Commissioner proposes to take concerning these case reports.

Thank you for your consideration.

Sincerely,

Daniel J. Manelli

DEPARTMENT OF HEALTH AND HUMAN SERVICES
OFFICE OF THE SECRETARY
WASHINGTON, D.C. 20201

GENERAL COUNSEL
Rockville, MD 20857

August 11, 1980

Daniel J. Manelli, Esq.
Bushnell, Gage, Reizen
& Byington, P.C.
1111 Nineteenth Street, N.W.
Washington, D.C. 20036

Dear Mr. Manelli:

This is in response to your letters of July 1 and July 22, 1980, to the Commissioner of Food and Drugs. You assert that Dr. Crout's prepared statement at the hearing before the Subcommittee on Oversight and Investigations, House Commerce Committee, resulted in the gratuitous revelation of a trade secret of your client, Blairex Laboratories, Inc. Specifically, you object to that portion of Dr. Crout's statement which disclosed, in your view, that your client's pending premarket approval application (PMA) is for a salt tablet that results in the preparation of only 15 ml. of solution at one time, thus revealing the size of the tablet. You also request a meeting with the Commissioner to discuss this matter.

I apologize for the delay in responding. As you are aware from numerous phone conversations since the date of your letter, members of the Bureau of Medical Devices, the Commissioner's staff, and this office have been variously involved in the consideration of both your client's PMA in particular and the larger issue of salt tablets for contact lens use in general; this has taken some time. After looking into the matter, however, it is my view that Dr. Crout's statement did not result in the unauthorized or illegal disclosure of your client's trade secret.

First, your client is not mentioned by name in Dr. Crout's statement. Therefore, the knowledge that it is your client's PMA that was discussed by the Ophthalmic Device Section (the "panel") on February 11 and June 2, 1980, must be derived from another source.

Second, I do not agree that Dr. Crout's reference to "15 ml." of solution has disclosed information unique to your client. On the contrary, the 15 ml. size unit-dose for saline for disinfection of soft contact lenses is not new to your client's PMA. During the course of the June 2, 1980, meeting of the panel, there was discussion of the "unidose"

(sic) solution approach to the problem of disinfection of soft contact lenses. This approach had been the subject of approvals by the Bureau of Medical Devices in 1979 and 1980. Those products are now on the market. And, As Dr. Talbot stated during the June 1980 session of the panel, that was a precedent for the application then being considered, the PMA of your client.

Further, the benefits of a 15 ml. unit-dose for disinfection of contact lenses, as opposed to the former large volume bottles that became "old, dirty, and badly deteriorated," is discussed in the August 1979 issue of Contact Lens Forum, pages 91-95.

It thus seems that the 15 ml. unit-dose size is a concept that has been discussed within the industry and before the advisory panel, and approved by the Bureau prior to Dr. Crout's testimony before the Subcommittee. Dr. Crout's testimony therefore did not illegally disclose trade secret information of your client.

In view of the foregoing, and the fact that the Blairex application has been approved, there no longer appears to be a need for a meeting with the Commissioner.

Sincerely yours,

Nancy L. Buc
Chief Counsel

Mr. GORE. Here is a press release by a company that has a big stake in the profitability of these more expensive preserver solutions. This was put out a week after our last hearing.

It says, "Recently the National Registry of Occular Side Effects reported that more than 200 cases of corneal infections were seen in patients using salt tablets."

Those 200 cases are fictional, really, aren't they? Isn't that obvious?

Mr. GOYAN. It is not obvious to me. Certainly it is questionable, and we are taking steps to get that removed from the record.

Mr. GORE. If they are not scientific—you have just testified they are not scientific—should they be in a scientific journal, then?

Mr. GOYAN. No, I don't think that I should be, and we are taking steps to get that removed from the record.

Mr. GORE. You wrote the subcommittee and said that you asked somebody with responsibility for the Registry to write a letter to the editor discussing the problems in interpreting data. Why not take steps to expunge those cases?

Mr. GOYAN. That is exactly what we intend to do, to ask that those be expunged until we get more scientifically justifiable data.

Mr. GORE. Dr. Crout.

Dr. CROUT. Expunging in the sense of removing those cases from the computer file; it doesn't have to take place. They never were in the Registry in the technical sense.

When Dr. Frumfelder wrote his article, he referred to a survey made by the Registry.

Mr. GORE. We got them from the Registry themselves. They are listed in the Registry.

Dr. CROUT. That is news to me, then. My understanding from our staff is——

Mr. GORE. This press release from Bausch & Lomb says they are in the Registry, and they are telling doctors all over the country that this is in the Registry.

Dr. CROUT. That is from a publication written by the Registry which should be corrected. I am saying that expunging is not what is needed. The thing that is needed is a publication from the Registry indicating that survey is not a scientifically valid one. That publication has been agreed upon by Dr. Frumfelder and ourselves, and we expect the text of it to be sent to the Journal in the next few weeks.

Mr. GORE. Now FDA also has a number of ways to get information to the public about health-related matters, talk papers, and other such media. Do you intend to tell the public through some other means that this data is probably not true?

Dr. CROUT. I don't think we have considered that. We have to draw a distinction between whether those data support the point and whether there is a risk with salt tablets. There is other information, some which will be published in the future, and the documented eye infections related to salt tablets. We don't want to give the impression, any of us, that salt tablets are necessarily free of risk. That is a different subject and there is other data than the Registry raising that concern.

Mr. GORE. We went through all the data we could find and that the medical community could find at the last hearing, and of course we welcome any additional data. But specifically what I am asking you to do is to disavow Dr. Scafidi's infamous notebook. Can you do that?

Dr. CROUT. We can, and should, but in so doing, the message necessarily is that salt tablets are risk free. The point is, that is not a scientifically documented study.

Mr. GORE. That is a charitable description.

Dr. CROUT. On the other hand, the point he is making is not necessarily wrong.

Mr. GORE. Is it necessarily right? Do you believe it is right?

Dr. CROUT. There is some very clear evidence; yes, some that will be published in the near future, that salt tablet solutions, at least the old ones, clearly cause some cases of corneal ulcers. Dr. Louis Wilson, for example, has told me of this on the phone, and is writing a letter to the effect and will publish cases where cultures from the eye and cultures from the bottle of solution produced the identical bacterium with the identical steriotype. Some indications of pseudomosis has occurred in users of these salt tablets.

Mr. GORE. This name that you have mentioned is the only one Dr. Scafidi could come up with in his list of 200 when he testified up here. For you to say, even though I disavow Dr. Scafidi's notebook and even though this notebook is half fable—that is my word, not yours—he may be right because some doctor talked to me on the telephone and it was the one doctor that Dr. Scafidi could cite by name who talked to him on the phone.

Dr. CROUT. He is a noted scholar in the field and has cases which I think both Dr. Scafidi and I are referring to in publications at the present time. So the point is, I think, scientically demonstrated. How common is impossible to tell.

Mr. GORE. Well, again, you say scientifically demonstrated. It has not been scientifically demonstrated to anybody yet except in this telephone call. There were other cases examined in the last hearing. There are a lot of problems that can occur both with salt tablets, saline solutions, and with any other system which is adopted. When you examine some of the other cases we looked at, you will find the salt tablets themselves were not responsible. There is going to be misuse of any kind of system that you have. So I will just say to you, before I accept his data as scientifically established, I would like to see it in printed form so that the procedures, techniques can be reviewed and analyzed. I will not take the word of anonymous reported telephone calls to people at FDA as a scientific basis for decisions.

Dr. CROUT. I agree with that. You should also know that, to our knowledge, there have not been similar reports associated with the premixed salt solutions; to date, serious corneal infections have not been reported in the premix solutions, only irritation of the eye.

Mr. GORE. There have been a lot of reports as to the preserved saline solution?

Dr. CROUT. Yes, but no infections.

Mr. GORE. What exactly, Dr. Goyan, are you going to do to expunge the public record of these 200 cases?

Mr. GOYAN. We will be sure it is out of the computer system and we will make sure that a letter is before the Journal within 2 to 3 weeks. Now, how quickly they publish it I don't know.

Mr. GORE. With the FDA's name on it?

Mr. GOYAN. Yes. We do believe the new salt tablets are a good system and doesn't have the problem of the past. It is tricky to say we are concerned about the old salt tablets but not the new ones.

Mr. GORE. That is why it is important to set the record straight. You are convinced that the new salt tablet system that you have approved is completely and totally safe for consumers to use, and it is cheaper than to use any other system if it is used right?

Mr. GOYAN. Yes.

Mr. GORE. Are you going to take any steps to counteract the misleding information put out by manufacturers of the premixed solution?

Mr. GOYAN. That matter is before the FTC, which rules in this matter. In addition, we will give consideration as to whether we will put something in our consumer magazines.

Mr. GORE. The medical community and the public at large is being given a great deal of misleading information about salt tablets by companies making the premixed solutions. They are telling people they are unsafe. I hope the FDA, in light of its earlier role in this whole fiasco, would take an agressive attitude in trying to correct the record insofar as the public is concerned as well.

Your testimony was that reviewers in the agency—and the word "reviewers" is in quotes—on page 6 of your testimony—let me read your statement here:

Reviewers in the Agency believed then, and still believe, that salt tablets which were then used to make up unpreserved solutions for disinfecting the soft lenses carried substantial risks, especially when they were improperly handled.

Isn't that Dr. Scafidi and Mrs. Bruch?

Mr. GOYAN. Yes, it is. However, I would add that personally it is theoretically possible to have pseudomonas growing if you don't oil it and if you put it in a cornea it could lead to infection.

Mr. GORE. Wasn't Mrs. Bruch's testimony that the salt tablets were dangerous when mishandled?

Mr. GOYAN. If used perfectly, they work perfectly.

Mr. GORE. You say reviewers in the agency believe that salt tablets then used carried risks, especially when mishandled. That is an inconsistency, is it not?

Mr. GOYAN. It is a slight one.

Mr. GORE. You want to correct it?

Mr. GOYAN. I think there is some small risk anyway.

May I add, Mr. Chairman, subsequent to your last hearing, I asked our Acting Deputy Commissioner to work with a group within our Office of Science at FDA to look at the decision originally made and they came out with that position.

Mr. GORE. Let me take this opportunity to say that I think you acted commendably in getting salt tablets back on the market very quickly after our last hearing. I appreciate that and I know a lot of consumers who can spend less money as a result appreciate that too.

But let me clarify why I am pursuing this matter and then I will go on to another matter.

I think if we are going to make this Government work properly and if we are to attain any degree of confidence on the part of the American people in our ability to regulate in an area that clearly needs some protection for the public health in devices that you put on your eyeball, then we are going to have to be very thorough in ferreting out misconduct of the kind I believe occurred in this case.

Here we have two highly paid professionals at the FDA who established a close personal relationship with a single company in this field and then showed favoritism to that company in a way that profited them greatly at great expense to the consumers of soft contact lenses.

I don't think it is sufficient just to rectify the earlier mistake; I think it has to be rectified completely. Not only should salt tablets go back on the record, but also the record should be made clear. The system should be made to work properly and the people responsible for this, I think, should be held accountable for it.

I would hope that procedure moves forward as well.

Now, let me move on to the example that we are also investigating here today. In your prepared statement you say "We recognize our obligation to assure that to the greatest extent possible, all applications were reviewed using the same ground rules."

Now, we heard from Automated Optics this morning, this claim that the ground rules were not uniformly applied in the case of Soft Lenses and its supplier, Burton-Parsons. I would like to address some of the interesting irregularities in their application.

I would like to put into the record at this point the chart and chronology I referred to earlier and related documents. Let me give

you a copy of this chart we have prepared here which will make it a little easier to follow what we are talking about.

[Testimony resumes on p. 44.]

[The documents referred to follow:]

COMPOSITION OF THE THREE LENSES

BUTTON SOURCE	I From Automated Optics	IIa From Burton-Parsons	IIb By Soft Lens Itself
Major Chemical Ingredients by Percent			
HEMA	80*	90	95
Ingredient 2	20	0	0
Ingredient 3	0	10	less than 5
Ingredient 4	0	0	above zero**
Name of Lens	Hefilcon	First Hedfilcon then Bufilcon	Bufilcon A

* Numbers are rounded but representative to demonstrate differences

** Can significantly affect water content

Prepared 12/11/80

CHRONOLOGY - HYDROCURVE II

May 2, 1975

Testing started on human subjects with the Hydrocurve II lens.

June 13, 1975

Soft Lens Inc., files an amendment to IND (Investigational New Drug) #7898. The amendment sets out the protocol for human testing.

Their filing states that Hydrocurve PHP made with the Automated Optics polymer is "chemically indistinguishable and physically identical" to the Hydrocurve II lens made with the Burton-Parsons polymer. (See: interview of FDA chemist dated December 4, 1980, he states that is a untrue statement.)

July 11, 1975

Soft Lens Inc., files its NDA #17-752 (New Drug Application) for the Hydrocurve II lens. Application states that Hydrocurve I and Hydrocurve II are "essentially chemically indistinguishable and physically identical". The NDA states that studies were being performed on human subjects for approximately 3 months.

August 6, 1975

FDA medical officer, Arnauld Scafidi signs-off on the amendment to the IND that was filed June 13, 1975. Scafidi states that the chemistry of the amendment is under review (see interview of chemist of December 5, 1980, chemist claims he never reviewed amendment to IND.) Scafidi recommends that clinical studies be initiated.(note: that they were started on May 2, 1975.)

February, 1976

FDA issues a non-approvable letter to Soft Lens Inc., stating that their tests on 23 human subjects is not enough. FDA asks them to submit more studies.

June, 1976

Soft Lens Inc. files an amendment to the NDA #17-752 filed July 11, 1975, the amendment states that the button once made at Burton-Parsons is now being made by Soft Lens, Inc.

The amendment also states that 314 human subjects were tested. (using the polymer made at Burton-Parsons.)

(Note: The interviews with FDA chemist dated December 4 and 5, 1980. He states that according to his review notes the polymer changed when it was manufactured at Soft Lens Inc.--that they first manufactured a button in May 6, 1976 and a lens from that button on July 8, 1976. He concluded that the "human tests were done only on the first polymer"--not the polymer ultimately approved.)

November, 1976

Soft Lens Inc. files clinical data (104 human subjects) to support use of cold chemical solutions (Burton-Parsons solutions) for use with Hydrocurve II lens.

February 12, 1977

Microbiologist's review of NDA #17-752 drafted and signed by Mary Bruch. Bruch states in the opening paragraph in her review:

> "This is an NDA for a lens which is the same as the marketed Hydrocurve Lens but the polymer is produced by Soft Lens, Inc. This lens appears to have a lower rejection rate for buttons and probably is a more highly purified material."

February 14, 1977

Pharmacologist Review of NDA #17-752. This memo is drafted and signed by Norma Browder and initialed by Merle Gibson, M.D. Dr. Browder states in her memo:

> "Sponsor states that the material used in their Hydrocurve (Hedfilcon A) contact lens (the subject of this NDA) is physically identical and chemically indistinguishable to the material now being used in the fabrication Hydrocurve Contact Lenses (subject of NDA #17-367)."

March 13, 1977

Scafidi drafts "Summary Basis of Approval" which states "the bufilcon A hydroplubic lens is being substituted for the hefilcon A contact lens. The materials is being manufactured by the sponsor and is essentially physically identical and chemically indistinguishable from the material now being used for hydrocurve contact lenses." This memo was seen by Bruch, Browder (pharmacologist) and Casola (chemist) and Kochert (the reviewing chemist).

The memo also states that 458 subjects were used to study this product--note: June 6, 1976 and November 1976 in chronology--there may have been only 104 subjects tested with the polymer being approved and those 104 subjects were specifically testing the cold chemical solutions.

March 31, 1977

FDA approves the Soft Lens Inc., application declaring Hydrocurve II lens a safe and effective product. Approval letter signed-off by Scafidi, Bruch, Browder (pharmacologist), Kochert (chemist), and Gibson (supervisor of the review team).

IND AMENDMENT, CONTINUOUS CURVE

June 13, 1975

AMENDMENT TO IND 7898

Merle Gibson, M. D.
Division Director
Division of Anti-Infective Drug Products
Bureau of Drugs
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Dear Dr. Gibson:

Reference is made to IND 7898 for Modified and Crosslinked Hydroxyethyl Methylmethacrylate as a Soft Hydrophilic Gel Contact Lens.

We are presently considering an alternate supplier for the material, modified and crosslinked poly (2-hydroxyethyl methacrylate) used in the fabrication of HydroCurve^{tm} Lenses (NDA 17-367).

Our present supplier is Automated Optics, Inc. (Englewood, Colorado 80110). Our proposed alternate supplier is Burton, Parsons & Co., Inc. (Washington, D. C. 20027), which is now able to produce a product which is physically identical and chemically indistinguishable by normal physical acceptance tests and chemical analysis, tentatively called "hedfilcon A" which is also a modified and crosslinked poly (2-hydroxyethyl methacrylate).

Burton, Parsons & Co., Inc., is submitting a Drug Master File describing the manufacture of hedfilcon A.

We consider hedfilcon A and hefilcon A to be generically the same when used in contact lenses but plan to do extensive studies in addition to referring to NDA 17-367.

Please find enclosed:

1. Chemical and physical tests comparing hedfilcon A and hefilcon A, showing that they are physically identical and chemically indistinguishable using normal physical acceptance tests and chemical analysis.

RECEIVED
JUN 16 1975
BUREAU OF DRUGS
HFD-140

SOFT LENSES, INC.
8006 ENGINEER ROAD, SAN DIEGO, CALIFORNIA 92111 (714) 277-9522

2. Pharmacological studies.

3. Microbiological studies.

4. The Clinical Protocol, which will be used to confirm that HydroCurve™ Contact Lenses fabricated from hedfilcon A have the same safety and effectiveness as HydroCurve™ Contact Lenses fabricated from hefilcon A.

Sincerely,

Donald Brucker

Donald Brucker, O.D.
President

DB:fs
Encl.

CONGRESS OF THE UNITED STATES
HOUSE OF REPRESENTATIVES
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS
OF THE
COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE
WASHINGTON, D.C. 20515

MEMORANDUM

Date: December 11, 1980

To: Files

From: Susan Lea[illegible]

Subject: Meeting with Bill Kochert, Chemist, FDA, December 4, 1980

Elliot Segal and I met with Bill Kochert, on December 4, 1980. I started the meeting by asking Kochert what were the difference between "Hydrocurve I PHP" lens approved in April 1974 and Hydrocurve II lens approved in March 1977. He started out by saying that the lens were very similar for all practical purposes. I asked him to show what the differences were between the two, specifically, if he could draw the chemical structure of the two polymers. He wasn't sure of the chemical structures and began to search through his notes to find something on the structure of Hydrocurve I.

I switched the topic from the differences between Hydrocurve I and II to the differences between the two polymers compositions of Hydrocurve II. I referred him to his chemist review, one dated February 1976 and the other dated January 1977. I stated that I noticed a difference between the chemical compositions and water contents of the two polymers. Specifically, that the proportion of the major components were different.

Referring to his chemist reviews he noted that there was definitely a difference between the polymers that were submitted at different times to the application for Hydrocurve II. He stated that normally the polymer is not changed without putting in a new New Drug Application (NDA).

We went to our discussion of the comparison of Hydrocurve I and II. He stated that the minor ingredients were different and, that a polymer chemist can easily switch around the composition of polymer. He said the polymer of the lenses are often changed to get around the patients.

I asked Kochert to specifically discuss the differences in the chemistry between Hydrocurve I and II. He stated that chemically it was different--very different. He looked at a structure of Hydrocurve II and I and noted the chemical structure were definitely different.

Further, he said that the II had differences in stability, tearing resistance.

We discussed differences between the Hydrocurve II first polymer which we named Hydrocurve II (A) and the second Hydrocurve polymer which we termed Hydrocurve I (B).

I asked why the polymer was changed during the approval process. He said that he didn't know why that normally it is not changed and that once the IND is started the product is pretty well set.

I asked if he knew of the human tests were done on IIA or IIB. He said he didn't know but he would check. (See telephone memo dated December 5, 1980).

I asked about the use of the USAN (the proprietary name) for Hydrocurve I and II--specifically that Hydrocurve I was called hefilcon and Hydrocurve II which had the proposed name of hedfilcon. I asked him whether or not the proposed by Burton-Parsons would be misleading that I and II weren't different. He said he didn't think it was misleading but was very similar and you didn't want them to be confusing to physicians--so that's why the proposed name for Hydrocurve II was changed from hedfilcon to bufilcon. He said we wanted to make sure the public and physicians know that they are two separate products.

I then asked him to compare Hydrocurve I with Hydrocurve II and Hydrocurve II(A) with Hydrocurve II(B). He said that between I and II there were greater differences than between II(A) and II(B).

He said that the Hydrocurve II(A) button was made by Burton-Parsons. Whereas II(B) button was made by Soft Lens, Inc.

I asked him when II(B) was first made - He said he would check. (see telephone memo of December 5, 1980).

Bill and I went through the composition between of I, IIA, and IIB. He said that I had 80% HEMA and 20%; IIA had 90% HEMA and 10% ( ) and IIB had 95% HEMA and 4.4% ( ) and that there was a change in the water content of IIA and IIB from 54% water content to 45% water content.

I referred Bill to the cover letter to the IND amendment for Hydrocurve II made by Burton Parsons. I read one of the opening paragraphs of the letter which stated that the Hydrocurve II button made by Burton Parsons and Hydrocurve PHP made by Automated Optics were chemically indistinguishable and physically identical. He said this could not be a true statement.

A showed him the Scafidi memo which reviewed and recommended approval of the IND amendment. The memo states that the chemistry in the amendment was under review. I asked if he didn't raise some question about this statement in the application to the medical officer or the rest of the review team. He said that "if I didn't bring it to the attention of the medical officer, I should have". (see telephone memo of December 5, 1980).

MEMORANDUM

DATE: December 9, 1980

TO: Files

FROM: Susan Leal

SUBJECT: Telephone Conversation with Bill Kochert, Chemist, FDA December 5, 1980

He opened the conversation saying he was calling to answer questions that I had at our last interview.

He said that regarding the June 13, 1975 amendment to the IND, he did not review the chemistry nor did any other chemist in the division.

I stated that Scafidi wrote in a memo that the chemistry is the IND was under review. He reiterated that the chemistry in the IND amendment was not reviewed.

He said that regarding the change in composition in the Hydrocurve II lens, he has not record of this change being discussed in-house. And, recalling from memory, it was not discussed.

The conversation moved to a discussion of the timing of change in polymers for the Hydrocurve II button. He said that soft lens made its first button for itself on May 6, 1976 and the first lens from this button on July 8, 1976. He said that the polymer changed when they began making it for themselves.

He said that the file showed that the first record of the change was the submission to FDA of June 6, 1976.

He concluded that because the human tests were done before the June submission (tests on solution were done in November, 1976), "human tests were done only the first polymer".

Mr. GORE. As you will note from this chronology and as admitted in your prepared testimony, the tests were done on human subjects before the application for testing was filed with the FDA.

My first question is, don't you feel this is in itself a serious breach of your safety standards?

Mr. GOYAN. Did that relate to the IND?

Mr. GORE. Yes, it did. You will note from the chronology—and you said this in your prepared testimony, that the tests——

Mr. GOYAN. This is not the chronology; this is the chart.

Mr. GORE. The first entry on the chronology is May 2, 1975. The human testing, the testing on human subjects began before the application for human testing was even filed with FDA.

Now, according to the established procedure at FDA, if you are going to conduct human tests on a device that comes into contact with the eye, you have to first get approval for those human tests by certifying that the protocol and material to be tested is of the kind that will not do irreparable damage to the test subjects.

Isn't it a serious breach for testing to begin before the application is filed?

Mr. GOYAN. It is a breach. They did have an IND on file for the hydrocurve lense. They were new at this game in dealing with our agency. When they became aware they could not use the material previously used, they filed the IND with us.

As you say, it was a breach.

Mr. GORE. They alleged it to be similar. We heard testimony earlier as to the vast differences between the two lenses.

Let me refer now to the chart which I have given you relating to the composition of the three lenses.

The first two, lenses Nos. 1 and 2(a) on the chart are the two that we saw described on the blackboard earlier.

Is it your belief that these are chemically indistinguishable from each other?

Mr. GOYAN. Certainly not. They are, however, quite similar.

Mr. GORE. Of course, those are value-laden words. They were different enough to get different patents, were they not?

Mr. GOYAN. Indeed they were and we required they be tested independently.

Mr. GORE. We are going to get into that, but to wrap up the question on human testing, section 505 of the FDA Act appears to have been violated by that procedure of going forward with the human testing before filing an application for the human testing and FDA evidently took the assertion by this company at face value and didn't inquire further.

Is that too harsh a judgment? Would you like to comment on that?

Mr. GOYAN. That is fairly close to accurate.

Dr. CROUT. I want to draw a distinction between filing an NDA and filing an IND and filing a protocol under the IND.

At that time and indeed even now, we permit new formulations to be explored clinically under the same IND. So the technical violation from our perspective was not the failure to submit a new IND. It was the failure to submit protocol and notify us of that before they began the study.

But no review of that protocol is required. The firm may go ahead and begin studies under the protocol as soon as it is submitted.

Mr. GORE. We think there were probably violations in both. We will get into it in some detail.

Dr. CROUT. In anticipation of that, I feel at least there was a violation in their failure to submit the protocol but no violation in their failure to get a new IND.

Mr. GORE. We will go into that and we are going to outline the role that these two personalities featured in the last hearing played in the decision itself.

Now, to wrap up this point, it is your testimony, Dr. Goyan, that these two lenses are chemically distinguishable or indistinguishable?

Mr. GOYAN. Chemically distinguishable.

Moving in the chronology to the item marked June 1976, which is at the bottom of that page, it appears the human tests were done on some lenses but not on the lense that was ultimately approved, even though the applicant states they are the same, the chemist

review, and FDA chemist who filed a review in February 1977 shows the different compositions of the lenses.

Mr. GORE. Now is it standard operating procedure to test one product and then approve another?

Mr. GOYAN. Well, in cases where there are slight changes, that has happened. In this case there were relatively minor changes. It was caught, as you say, by the FDA reviewing chemist but not considered to be of sufficient importance by him to bring to the attention of the other reviewers for their concern.

Mr. GORE. The supervisor with responsibility over that chemist's review was you, wasn't it, Dr. Gibson?

Dr. GIBSON. Actually Dr. Kochert, he is a chemical supervisor, Mr. Kochert was the chemist.

Mr. GORE. Did you look at the review?

Dr. GIBSON. His final review? He had three reviews. As a matter of fact, his final review was made March 1, 1977. His No. 2 review actually referred to the change in the chemical content which was considered to be fairly minor and was covered in his second review in which he identified the difference in the chemical formula from the initial submission of July 11, 1975, which was the Burton-Parsons material.

The June 1976 submission was the Soft Lense submission made in San Diego, Calif.

Mr. GORE. This is a complicated area. There are two ways to approach it. One is on an absolute basis, to look at whether the decision you made was correct or not in looking at this isolated case. The chemist said this is not chemically indistinguishable; the company testified it is chemically indistinguishable. The chemist looked at the formula, looked at the claim and said it is chemically distinguishable, in fact there are significant differences in the chemical structure. That decision came to you and you said, we will just let it go.

Dr. GIBSON. The final package came to me. We noted there were differences in the content. This is in 1976. By that time we had done other reviews and some were approved. There were seven or eight more applications for soft contact lenses in between the initial submission and the second submission.

All of these had clinical studies with some exceptions and we saw no unusual safety problems in rather significant variations in the chemicals and water content. It varied from 38 to 54 percent. In fact, this question was brought before the Optometric Device Panel, March 7, 1977, as to what changes would indicate new clinical studies. They felt the wide range with which there was experience at that time should not require the necessity or doing additional clinical studies.

In other words, one quote was "Why charge the firms the expense of reinventing the wheel?" All of this was going on at that time.

We had gathered more experience; we were not concerned at that time with the slight differences although the water content was the same as the others, as far as the safety to humans was concerned—we were very concerned with the quality control.

Mr. GORE. OK. As I started to say, there are two ways of looking at this. The first is to look at it in the absolute context, was your decision correct in this specific instance.

The other way, and the more important to look at it, is to compare the decision that was made in this instance where Burton & Parsons was involved, to the decision made in other cases, where similar requests were made to FDA. Specifically, let's look at the decision which was made when Automated Optics asked for the right to do exactly what Burton & Parsons did. In both instances Soft Lenses was the company asking for approval, but in the first case, Burton & Parsons was the contractor.

In the second case, Automated Optics was the contractor.

Now, in the second case, Automated Optics, through Soft Lenses, asked for the right to forgo this lengthy procedure, to start over from square one with all of the human testing, based on their assertion that the differences between their new material and the original material already approved, was very slight, indeed, the differences were far less than the differences between the first lens and the lens approved made by Burton & Parsons.

Burton & Parsons came and made that request and FDA said fine, you don't have to go through this long testing procedure, but when Automated Optics material came in for approval they were told no, you have to go back to square one, start over again, lose a lot of time, and perform all of these lengthy scientific tests even though Burton & Parsons was not required to do so.

Mr. GOYAN. May I comment on that?

Mr. GORE. Yes.

Mr. GOYAN. I am very puzzled by that statement and the statment that was made by the previous witness, because clearly Automated Optics has never brought anything to us, they are not the sponsor.

Mr. GORE. I try to make it clear that Soft Lenses was the person, the entity making the request in both instances. In the first case, their contractor was Burton & Parsons. In the second case their contractor supplying the material was Automated Optics. What required the new testing was the material supplied by Automated Optics.

Mr. GOYAN. Well, I am still confused because the Optics I came in first, it was one——

Mr. GORE. Let's go to the chart, this is confusing. I think you will do something about this when you see exactly what happened, Commissioner.

Look at this chart here. Now, No. 1 is the first lens. All three of them come from Soft Lenses.

Mr. GOYAN. Right.

Mr. GORE. The contractor supplying the material for lens No. 1 is Automated Optics?

Mr. GOYAN. Right.

Mr. GORE. They go through a lengthy scientific procedure and get approval?

Mr. GOYAN. Yes, roughly 11 months.

Mr. GORE. Now, this chart describes—the third lens on this chart refers to a lens manufactured by Soft Lens itself?

Mr. GOYAN. Right, after getting licensed by Burton & Parsons, right?

Mr. GORE. We are going into this. Forget the chart. Let me go through this. The first lens was submitted by Soft Lenses, Inc., using material supplied by Automated Optics?

Mr. GOYAN. Right.

Mr. GORE. They go through a lengthy scientific testing procedure and get approval?

Mr. GOYAN. Right. Bear in mind that was the first time that particular polymer had been brought before us. It was the second generation.

Mr. GORE. OK. The second lens is brought to the FDA by Soft Lenses, Inc., again using material supplied by Burton & Parsons?

Mr. GOYAN. Correct.

Mr. GORE. Soft Lenses says don't make us go back through this lengthy scientific testing procedure.

Mr. GOYAN. That is right, they did, but we made them do it.

Mr. GORE. With a very shortsighted process.

Mr. GOYAN. No.

Mr. GORE. With much fewer human studies. They were first asked to do 23 studies and then you said no, 23 is ridiculous, you are at least going to have to do how many? How many did they end up doing?

Dr. GIBSON. The initial submission was one investigator with 23 participants. It was felt to be insufficient evidence, clinical evidence. They were told to do additional studies and they did. We have a list of the investigators and the number of participants they did.

Mr. GORE. How many, do you know?

Dr. GIBSON. Yes, sir; I can tell you.

Mr. GORE. It was significantly fewer than usually required?

Dr. GIBSON. They did—the sponsors voted a total of 558 participants in this study, and there were 12 investigators.

Mr. GORE. What was your response?

Dr. GIBSON. My response was there were 458 participants in the second study.

Mr. GORE. Now, that was for lens 2–A, right?

Dr. GIBSON. That was done on lens 2–A but was submitted in June 1976, at which time they informed us they had changed their manufacturing from Burton & Parsons to Soft Lenses.

Mr. GORE. How many human studies were done on lens 2–B on the chart, the one that Soft Lenses finally sold to the public?

Dr. GIBSON. None.

Mr. GORE. Why not?

Dr. GIBSON. Because I don't know exactly why not. It is assumed that the difference between the two polymers was not significant.

Mr. GOYAN. That is 2–A and 2–B?

Dr. GIBSON. 2–A and 2–B. As I mentioned before, there has been much more experience with clinical studies and safety data over that period with seven or eight different lenses having been reviewed.

Mr. GORE. Well, why, a year later, when this other company came in and asked to use the same shortcut procedure, were they

told that the slightest change would require them to go back to square one and start all over again?

Dr. GIBSON. I cannot answer that because I am not aware of that meeting. I would have to check.

Mr. GORE. Dr. Crout, were you in that meeting?

Dr. CROUT. No, I was not, and I might add at this point I am baffled by it. We have an appeal system in the Bureau by which any firm feels if they have gotten a bad decision they can get a hearing on that.

Mr. GORE. Who was in that meeting?

Dr. CROUT. I have no knowledge of that. They come back to the Division Director, they come back to the Director of the whole office or they come back to me, and none of us have ever had an appeal on this matter brought to our attention by Automated Optics or any other firm.

Mr. GORE. The companies in this field have gotten a little frustrated with the procedures at FDA and with the assertion in the industry that Burton & Parsons had the inside track and that others were held back.

Now, Doctor, do you know who was in that meeting where this company was told that they had to go back and start over again?

Mr. GOYAN. That is a statement I continue to find mystifying because of the fact they have never sponsored a——

Mr. GORE. Where Soft Lenses was told?

Mr. GOYAN. I don't believe.

Mr. GORE. If they used Automated Optics material, they would have to go back and start the testing all over again.

Mr. GOYAN. Is there any documentation that meeting ever took place? We don't know anything about it.

Mr. GORE. We just had testimony on it here.

Mr. GOYAN. I understand.

Mr. GORE. Today, according to the witness who testified, the people present at the meeting were Dr. Scafidi and Mary Bruch.

Mr. GOYAN. All right.

Mr. GORE. If the company chose to appeal, who decides the appeal, Dr. Scafidi or Mary Bruch understood the former procedure.

Dr. CROUT. Our appeal system follows the usual procedure of institutions you go to.

Mr. GORE. Dr. Scafidi or Mary Bruch?

Dr. CROUT. I am sorry, Dr. Gibson. It should have been brought to Dr. Gibson's attention and if the outside party is unhappy with what they hear from Dr. Gibson they come back to Dr. Finkel and to me and then to the Commissioner. None of us have had any input on this from Automated Optics to this very moment.

Dr. GIBSON. I continue to be mystified about it because I can't understand why Soft Lenses would come in and want to make that change after they had already gotten the approval of their own lens they were manufacturing, 2-B. It was testified to earlier that it was reasonable for them to want to start producing their own. They have done so. Why would they come back on behalf of Automated Optics?

Mr. GORE. Well, you are here throwing some question on the fact that the meeting at all took place.

Dr. GIBSON. No, it may have taken place. I don't know. I would volunteer we will look into it and report back to the committee what happened.

Mr. GORE. Well, I would like to put into the record at this point a trip report filed after this meeting by the company that had the meeting. Let me see who was present. Representing FDA was Dr. Scafidi and Mary Bruch. Dr. Scafidi was seated behind the desk next to the window. Mary Bruch sat opposite to me. There was another gentleman in the room but I don't recall his name.

The conversation with Mary Bruch was commenced by Don Brucker. Who is Don Brucker?

Dr. GIBSON. President of Soft Lenses.

Mr. GORE. They were the formal applicant and they are trying to get approval for a system that use Automated Optics material.

Mary Bruch seemed to be the one in charge so all comments were directed to her. That is consistent with your understanding of the way this office operated, is it not?

Mr. GOYAN. I assumed there were only two people in the room.

Mr. GORE. It is consistent with the earlier testimony that we have.

They were told that if they wanted to, if they made the slightest change in the formula, they would have to go to square one and perform all of the tests all over again and not get any credit for the similarity to the previous material?

Mr. GOYAN. May I ask what the date on that was?

Mr. GORE. February 18, 1978.

Mr. GOYAN. All right, if that was done in 1978, then if that is an accurate presentation of the facts, I think that we are wrong. I do not think that we were holding to those sorts of standards at that time and I really wish it had been appealed.

Mr. GORE. So your testimony is that if the facts are as they are presented in this record, then Dr. Scadifi and Mary Bruch made the wrong decision?

Mr. GOYAN. I don't believe it was consistent with the policy in the division at that time. Am I correct?

Dr. GIBSON. I agree.

Dr. CROUT. I think we would like to, if we might, Mr. Chairman, leave the record open so we can see what our other files show on the record of that meeting and give it to you. I think I would also voice a note of caution as to whether they were told that.

Mr. GORE. Well——

Dr. CROUT. In quite that way, because many other manufacturers have gotten soft lenses approved since then.

Mr. GORE. Let me assure you we have searched your files pretty thoroughly and I don't think you will find it there, but you are welcome to look.

Dr. CROUT. OK.

Mr. GOYAN. We will give it a try.

Mr. GORE. We will hold the record open.

What has happened here is that two of your FDA employees developed a very close relationship with the executives in one of the companies that had entry into this multimillion dollar industry. This company got favored treatment whenever it came before FDA; in sharp contrast other companies competing with Burton &

Parsons, were slowed down, held back, told that they had to hurdle every single bureaucratic regulatory obstacle before they could get into the ball game and compete on even footing with Burton & Parsons.

That is what has happened and they somehow developed enough power and independence in this bureaucracy that they were able to do that without any of you gentlemen even being aware that the industry affected and ultimately the public was being harmed by their actions in this manner.

Is that a fair summation of what happened?

Ms. BUC. I think that is the one issue, the motivation of Mrs. Bruch and Dr. Scafidi from which we are essentially forbidden to inquire and what the Commissioner and the Bureau have been doing in the past months, literally in accordance with your instructions at the last hearing was to review as best they could the instance, to review as best they could what happened in a management sense, which you have heard some discussion of, but we are similarly not in a position to accept as a premise nor to disagree with the premise as to what Dr. Scafidi and Mrs. Bruch were doing.

That is in the hands, as you have stated earlier, as you instructed us, of the Inspector General. We don't know one way or the other. I think it is right that we not know at this juncture. And so any question that starts with the premise of Dr. Scafidi and Mrs. Bruch were doing something with or for Burton & Parsons is a question we can't answer, shouldn't be answering, you instructed us not to inquire into, so we are stumped on that.

Mr. GORE. I think that is quite proper for you to say and we should not interpret your lack of response to my last statement as in any way evidence of some kind of complicity in this whole arrangement or willful ignoring of the facts.

I do think, however, that the procedures which led to this travesty must be examined closely and changed. Let me move on.

This, again, is on the application for approval of the product, using the material of Burton & Parsons. Dr. Scafidi drafted the memo which served as the basis of approval. Now, let me say in preface that a number of times in this application there are claims that the product is essentially chemically indistinguishable and physically identical.

Dr. Gibson indicated that maybe the differences were not significant, and we will take a look at that briefly. It appears that the applicant, Soft Lenses, Inc., based this particular application, using the Burton & Parsons material, on the claim that the product was "chemically indistinguishable and physically identical."

In the summary basis of approval memo, drafted by Dr. Scafidi, it states that the product is essentially physically identical and chemically indistinguishable. However, according to the chemist's reviews of 1976 and January 1977, and the chart that we compiled, the Hydrocurve I lens made with the Automated Optics polymer, and the Hydrocurve II lens made with the Burton & Parsons polymer, are very different products.

Now, does the FDA take as gospel what the applicant states as a matter of general practice? Dr. Gibson, how did this happen?

Dr. GIBSON. What was your question again?

Mr. GORE. The company claims that the two materials are chemically indistinguishable. The chemists that looked at it in FDA say no, that is not the case, but Dr. Scafidi then writes a memo saying not that the differences are less than significant, not that the differences are of a kind that may not threaten human health, none of those judgments were made, Dr. Scafidi drafts a memo that says the company's original assertion that these two materials are chemically indistinguishable is true.

These two materials are chemically indistinguishable, they are identical, just as the company originally said. Even though the two chemists at FDA who looked at them said no, that is not the case, how did that happen?

Dr. GIBSON. We agree that they are not identical.

Mr. GORE. You now agree?

Dr. GIBSON. Well, I agree from the very beginning because Hydrocurve II is different from Hydrocurve I which we required a full NDA on Hydrocurve II. This apparently is an error.

Mr. GORE. So Dr. Scafidi's approval memo was in error there?

Dr. GIBSON. Well, the statement in this summary is probably in error.

Mr. GORE. Well, again, we established the relationship earlier and, again, this partiuclar error seems to be one that favors Burton & Parsons, does it not?

Dr. GIBSON. No, I cannot agree that it favors Burton & Parsons. But the time of approval of the Hydrocurve II lens, Soft Lenses was making its own material and had been since June 1976.

Mr. GORE. Well——

Dr. GIBSON. The initial material granted was Burton & Parsons material for which they got approval.

Mr. GORE. If this Burton & Parsons material could be approved, quicker, then Burton & Parsons was better off, right?

Dr. GIBSON. I don't know what you want me to answer on that.

Mr. GORE. I am simply trying to establish that the mistake, you characterize it as a mistake, that the mistake made by Dr. Scafidi assisted Burton & Parsons.

Dr. GIBSON. No, it did not. If you look at the average time for approval of all of the contact lenses, 22 months is the other limit.

Mr. GORE. If Dr. Scafidi had not made this mistake then and had not said that it was chemically indistinguishable, then the requirements imposed upon the Burton & Parsons material might well have been more rigorous, correct?

Dr. GIBSON. This may be a mistake in stating it but it did not affect the review or the submissions to the NDA.

Mr. GORE. Well, it did between the lens that was approved and the one that was subsequently sold to the public, there were differences there, too. But I am asking you a relatively narrow question. The decision, the "mistake", in quotes, by Dr. Scafidi, could have been expected to assist Burton & Parsons?

Dr. GIBSON. I cannot answer that yes or no because——

Mr. GORE. You have a material that, and FDA is asked to approve this material, soft contacts are going to be made out of the material, the material is made by Burton & Parsons, the material either has to be tested more rigorously or less rigorously, depending

upon how much reliance the company can place on the earlier tests made on another material.

The company claims they can rely a great deal on the earlier tests because their material is chemically indistinguishable from the earlier material that has already been tested.

The chemists at FDA say no, that is not the case, they are different. Dr. Scafidi says, yes, that is the case, these two materials are chemically indistinguishable. That decision ends up helping Burton & Parsons.

Dr. GIBSON. No, you are talking about 2-A and 2-B, not to Hydrocurve I, the first one, with Automated Optics and Hydrocurve II. I am confused, really.

Mr. GORE. It is really in both cases, but specifically, I am discussing the difference between the Automated Optics material and the difference between the Burton & Parsons material.

Dr. GIBSON. Dr. Scafidi is not the only one who was the reviewer on that, the only one who determined it. We had preclinical data that was reviewed. We had new manufacturing control reviews for that. We had a whole new NDA with new clinical data.

Mr. GORE. Well, the procedure allows these two people to exercise a great deal of influence on the outcome.

Dr. GIBSON. May I make one more statement?

Mr. GORE. Let me ask you this. If Dr. Scafidi had said the chemist has told me these two terms are different, therefore, a new IND is required, would that have slowed down the approval of the material supplied by Burton & Parsons?

Dr. GIBSON. The Burton & Parsons material was never approved. It was a soft lens material that was approved.

Mr. GORE. Using the Burton & Parsons material?

Dr. GIBSON. Data, clinical and preclinical data, yes.

Mr. GORE. Let me ask you again now, if Dr. Scafidi had said our chemist is right, these two materials are different, a new IND is required, as it was subsequently required of Automated Optics, if he had said that, then the approval of the soft lens application using the Burton & Parsons material would have been slowed down; is that correct?

Dr. GIBSON. If it had been decided that there was a difference enough to require another, a third NDA, it would have slowed it down.

Mr. GORE. If it had been, if the difference had been of a kind requiring a new IND?

Dr. GIBSON. Yes, sir.

Mr. GORE. Then it would have slowed down the approval of the lens using the Burton & Parsons material, and for that length of time—wait a second—you are trying to differentiate between 2-A and 2-B. Now, if it had been, if a new IND had been required?

Dr. GIBSON. Yes, sir.

Mr. GORE. Then the approval process would have been slowed down; correct?

Dr. GIBSON. Yes, sir.

Mr. GORE. OK. All right.

Now, how do you react as a matter of policy when a company comes in with a claim that its material is chemically indistinguishable from another? Is that assertion reviewed as a matter of

course? Is it challenged as a matter of course? Or is it accepted as gospel?

Dr. GIBSON. Not accepted as gospel. Along with that statement, and many companies make many statements that their product is the same but they have to submit the total information concerning the produce under study. That is determined by the reviewers. In this case the chemists.

Mr. GORE. But, the chemists said they were not chemically indistinguishable.

Dr. GIBSON. That is true.

Mr. GORE. Well, then the statement on the application was not true?

Dr. GIBSON. The statement as submitted by the firm was perhaps not completely the way we saw it. It may be the way they saw it on the tests that they did to determine it but our determination was different.

Mr. GORE. Let me ask the chemist to come up here. Mr. Kochert, we have a custom of swearing in witnesses. Will you raise your right hand?

Do you swear that the testimony you are about to give is the truth, the whole truth, and nothing but the truth, so help you God?

Mr. KOCHERT. I do.

TESTIMONY OF WILLIAM KOCHERT, CHEMIST

Mr. GORE. You can stay here, Dr. Gibson.

The statement in the IND that this material was chemically indistinguishable from the earlier material, was that statement true or false?

Mr. KOCHERT. False.

Mr. GORE. It was false?

Mr. KOCHERT. It was not true.

Mr. GORE. Thank you very much.

Mr. KOCHERT. You are welcome.

Mr. GORE. Now, Dr. Gibson, the statement was false. How come it is accepted as true?

Dr. GIBSON. It wasn't accepted in that a whole new IND was required.

Mr. GORE. A new IND was not required?

Dr. GIBSON. A new IND was not required, IND we have permitted variations in manufacture of products.

Mr. GORE. An IND, a new IND was not required based upon assertion that the similarities were close enough between the two products; is that right?

Dr. GIBSON. We have not necessarily required new INDs, especially in those days, for different dosage forms, for changes in manufacture, which this was, or even changes in suppliers.

Mr. GORE. Specifically, they were allowed to piggyback the earlier IND; is that right?

Dr. GIBSON. Well, I don't know if it is a piggyback or not but when an NDA is approved for other drugs, this was classed as a drug at that time, the IND remains open for further investigation, new indications, new variations, and if an amendment is added to the IND, I suppose you could call it a piggyback.

Mr. GORE. Let me ask the chemist to pull a chair up there. I want to ask you another question.

I would like you to compare the chemical differences between the Automated Optics material and the Burton & Parsons material, on the one hand. Do you know that comparison?

Mr. KOCHERT. Yes, sir; I know it.

Mr. GORE. That on the one hand and then the differences between the first Automated Optics material and the second application by Automated Optics, would you say that the differences between those——

Mr. GOYAN. Those are the ones we know nothing about.

Mr. GORE. The chemist knows about it.

Mr. KOCHERT. I think the question is not correctly stated. Can I go through that for you?

Mr. GORE. Well, let me try to correctly state it and let me ask for your assistance in correctly stating it. Are you familiar with the subsequent expression of interests by Automated Optics in getting an approval, with Soft Lenses the applicant, for a variation of the material that was first approved by Soft Lenses?

Are you familiar with that other material? He put it on the blackboard earlier.

Mr. KOCHERT. I would have to go back and look at my notes. I attended many meetings and things like this came up.

Mr. GORE. Let me just ask you a simple question.

Mr. KOCHERT. Right off the top of my head I am not familiar with it.

Mr. GORE. Let me ask you a simple question. Based upon what knowledge you have of these materials, would it be fair to say that the differences between Automated Optics, the original Automated Optics material and the subsequent variation of the Automated Optics material, that those differences were less than the differences between Automated Optics material and the Burton & Parsons material?

Mr. KOCHERT. I think that is a fair statement.

Mr. GORE. Thank you very much. You are excused.

Now, that is exactly what I wanted. Here is the sharp contrast, Dr. Gibson: Your FDA chemist has just testified that the difference between Automated Optics material and the later material they wanted to approve were less than the difference between Automated Optics' first material and the Burton & Parsons material.

Mr. GOYAN. Mr. Chairman, may I interject?

Mr. GORE. In one case, when Burton & Parsons was involved, a new IND was not required, Dr. Scafidi wrote a memorandum saying that it was chemically indistinguishable from the earlier material.

In the second case, Dr. Scafidi and Mary Bruch told Automated Optics that the differences were so significant, that they were going to have to file a new IND. That is unfair, inconsistent treatment by the FDA of two companies in this industry and one of them profits from it and the other one does not.

Dr. GIBSON. I don't know about the profit, Mr. Chairman, but, I agree, I am not familiar with the second Automated, with the Automated Optics meeting of February 1978, so I can't comment on it.

I think we have stated that it was a minor change under the policy at that time. We would not agree that a totally new IND would be required.

Mr. GORE. Say that again.

Dr. GIBSON. I am not familiar with the Automated Optics meeting of February 1978.

Mr. GORE. We put this memo in the record summarizing it. I think the upshot of it is clear. Burton & Parsons was allowed to short circuit the procedure and get a fast approval of a system that used this material when a competitor sought the same procedure. Even though the differences were less, they were required to go through a lengthy IND when Burton & Parsons wasn't.

Now, let me ask you about the——

Mr. GOYAN. We simply don't know whether that is true, Mr. Chairman.

Mr. GORE. You should. The people in charge of the FDA ought to know what is going on there.

I have a great deal of respect for you, Dr. Goyan, as you know, but a lot of what is going on in FDA is wrong. If the people in the Department can produce profit at the expense of legal procedures that should be followed to protect the public something is certainly wrong.

Mr. GOYAN. I would agree.

Mr. GORE. This is another lense that Soft Lense itself manufactured material for. This is yet another lense. Let me see if I can make this clear.

Soft Lense is again the applicant but this time it supplies its own material under the patent owned by Burton & Parsons. This material is different from the material that was approved using the Burton & Parsons material.

Dr. GIBSON. The Burton & Parsons material was never approved.

Mr. GORE. It was studied. This material made by Soft Lense itself was approved by FDA.

Dr. GIBSON. Yes. This was approved 2 months after the initial application. The human tests were done on a similar substance which was manufactured by Burton & Parsons during the early stage of the NDA.

Mr. GORE. We have a new supplier, a different polymer used; we have no IND, no NDA, no human test, and yet we have approval by the FDA.

Now, how did that occur?

Dr. GIBSON. As I indicated, the difference in the two polymers was such that it wouldn't affect the safety and efficacy of the new lense. That is the only answer I can give.

There is no written documentation on that, but that was the current belief at that time.

Mr. GORE. Again, Automated Optics, attorneys for which testified earlier, tried to get the same kind of treatment from FDA and they were refused. They were held back and not allowed to enter the marketplace and compete when this other company was allowed to do so.

Dr. GIBSON. As I say, I am not familiar with that. If they were not allowed to do it for a similar change, I think it was unfair treatment.

Mr. GORE. Well, we are going to put this material into the record. This will include all the back-up documents that are involved here.

I think the final record will show that favoritism did occur and that it would benefit the same company that was benefited by the mistake in decisions with respect to preserved saline solutions and salt tablets.

Together, these two instances form a pattern. The same company is benefited in both cases. The same FDA employees are involved in both cases. The public is damaged in both cases, both economically and I believe by being subjected to some unnecessary risks.

The FDA, in order to protect the public and fulfill its mandate, should not allow these kinds of instances of favoritism to occur.

With that, I would thank the witnesses for appearing here today. This hearing is adjourned.

[The following material was submitted for the record:]

August 6, 1975

MEDICAL OFFICER'S REVIEW OF IND 7898

Sponsor: Soft Lens, Inc.
8006 Engineer Road
San Diego, California 92111

Product and Synonyms: Soft hydrophilic Gel Contact Lens
hedfilcon A

Proposed Clinic Use:

Correction of visual acuity in persons with non-diseased eyes and a minimal amount of corneal astigmatism.

Structural and Chemical Name:

Modified and crosslinked (2-hydroxyethyl methacrylate) called "hedfilcon-A" manufactured by Burton, Parsons & Co.

Formulation, Route of Administration, Dosage, Duration of Use:

Soft contact lens to be applied topically to the eye and worn during the waking hours. The duration of wear is adjusted accordingly to each patient.

Related INDs, NDAs and Drugs:

NDA 17-367

porta - FLOW[R] Transfer Unit (basket))
HydroCurve[tm] Carrying Case)
Hydrotherm[tm] Patient Unit) To be used with the lens in cleaning and asepticizing
BOILnSOAK[tm] Solution)
Pliagel[tm] Sterile Cleaner (optional) or)
Soft/Mate[tm] Sterile Cleaner (optional))

Pharmacology: Under review.

Chemistry: Under review.

IND 7898

Clinical Studies:

The objectives of this study is to determine whether hedfilcon A contact lenses perform the same safety and effectiveness as hefilcon A contact lenses.

Brochure for clinical investigators and protocol for clinical guidelines will be the same as for NDA 17-367. The only change will be substitution of "hedfilcon A" for "helifon A". This protocol will apply to both new patient and to patients being switched from "helifcon A" to "hedfilcon A".

At least four investigators each following approximately 20 or more patients for up to six months will be utilized. There are no requirements as to age, sex, or occupation. The lenses are to be worn approximately twelve hours a day. All laboratory parameters will be met as is outlined in the October 1972 guidelines. No human data and no provisions for statistical data are present.

Summary:

A study is presented to show the safety and efficacy of the new manufacturer's product. The entire protocol is that of the previous NDA 17-367. The protocol is adequate.Since no new investigators are mentioned, it is assumed that the same investigators will be used.

Recommendation:

The clinical studies should be initiated.

... A Scafidi

Arnauld F. Scafidi, M.D.
Division of Anti-Infective Drug Products

cc:
Orig IND
HFD-108
HFD-140
HFD-140/CSO
HFD-140:AFScafidi:js
8/5/75

February 14, 1977

PHARMACOLOGIST REVIEW OF NDA 17-752

Sponsor: Soft Lenses, Inc.
San Diego, California

Drug: Hydrocurve (Hedfilcon A)

Category: Soft Contact Lens

Proposed Clinical Indication:

Correction of visual acuity in non-diseased eyes.

Related Submissions: NDA 17-367, IND 7898, and DMF 2475

Ancillary Products to be Used With Hydrocurve (Hedfilcon A) Soft Contact Lenses:

1) Porta-Flow^{R} Transfer unit (basket)
2) Hydrocurve^{tm} carrying case
3) Hydrotherm^{tm} Patient Unit
4) BOIL n SOAK^{tm} Solution
5) Pliagel^{tm} Sterile Cleaner (optional) or
6) Soft-Mate^{tm} Sterile Cleaner (optional)

I. Toxicity Studies:

A. Background information on previous preclinical studies perfor in support of safety of Hydrocurve^{tm} can be found by referenc to pharmacologist reviews of IND 7898 dated March 15, 1972 an NDA 17-367, dated January 24, 1973, Clyde G. Oberlander, NDA 17-367 dated March 4, 1974, J. M. Davitt and NDA 17-367 (Amendment to supplement #5) dated November 17, 1975 and July 12, 1976, Norma Browder.

B. NDA 17-367 (Hydrocurve^{tm} Contact Lens) was approved on April 30, 1974.

C. Sponsor states that the material used in their Hydrocurve (Hedfilcon A) contact lens (the subject of this NDA) is physically identical and chemically indistinguishable to the material now being used in the fabrication of Hydrocurve^{tm} Contact Lenses (subject of NDA 17-367). Toxicity studies submitted in support of Hedfilcon A are described in the sections which follow.

D. Twenty-One Day Ocular Irritation Study:

1) Lab. Performing Study: University of California
Berkeley, School of Optometry;
Dr. Robert Mandell

2) Item Tested:

Hydrocurve II Contact Lenses in conjunction with Pliagel Cleaner, rinsing with Boil n Soak and heating for 15 minu in soft lens heater.

3) Regimen:

21 day, 8 hour/day wearing in 2 groups of animals.

a) Normal eyes with disinfecting procedures.
b) Irritated eyes (0.1 ml of 10% Ivory Soap Slurry) with disinfecting procedures.
c) Lenses fitted on one eye only; contralateral eye served as control.

4) No. of Animals/Group: 6

5) Species Used: NZW rabbit

6) Lens Thickness Range: Minimum to maximum anticipated thickness.

7) Parameters Evaluated:

a) Cornea - degree of opacity & area involved.
b) Iris - inflammation.
c) Conjunctiva-hyperemia, chemosis, discharge.

8) Results:

a) Normal Eyes With Disinfecting Procedure:

All animals had minimum rxn. to lenses, beginning on the first day, reaching a maximum on the second or third day and subsiding to normal on the fifth day. Occasional minor irritation was noted throughout the test period.

b) Irritated Eyes With Disinfecting Procedures:

All animals had strong conjunctival rxn. to Ivory Soap irritation, reaching a maximum on first day, gradually reduced by the fifth day. This cycle was repeated following each application of irritant (beginning of 2nd and 3rd weeks of lens wear).

9) Conclusion:

a) Normal Rabbit Eyes:

Responded to wearing of gel contact lens with minimum short term conjunctival rxn. Investigator states this to be expected due to mechanical irritation of lenses.

b) Irritated Rabbit Eyes:

Recovery cycle only slightly delayed by wearing Hydrocurve contact lenses.

E. Continuous Wear - Ocular Irritation Study:

1) Lab. Performing Study: University of California
Berkely, School of Optometry
Dr. Robert Mandall

2) Item Tested: Hydrocurve II contact Lenses

3) Regimen:

21 days, 24 hour continuous wear in 2 groups of animals.

a) Normal eyes with Hydrocurve II contact Lenses for 21 days.

b) Irritated eyes (2 drops 10% slurry of Ivory Soap instilled 1 hour prior to lens insert and again after the 7 and 14 days with lens in situ) with Hydrocurve II Contact Lenses for 21 days.

c) Lenses fitted on one eye only, contralateral eye served as control.

4) No. of Animals/Group: 6

5) Species Tested: NZW rabbits.

6) Parameters Evaluated:

a) Cornea - degree of opacity & area involved.

b) Iris - inflammation.

c) Conjunctiva - hyperemia, chemosis, discharge.

d) Corneal respiration - polarographic technique of Hill & Fatt with recent modification by Fatt.

e) histopathology.

7) Results:

Gross Observation:

a) Normal Eyes With Hydrocurve II Contact Lenses for 21 Days:

Little or no reaction; several animals showed a minor acute keratitis (confined to limbus for both test and control eyes) attributed to lens irritation.

b) Irritated Eyes with Hydrocurve II Contact Lenses for 21 Days:

Several showed mild keratitis within the normal expect for test conditions.

Histopathology: Performed by Alan MacMillan, D.V.M, Univ. of California.

a) 3 animals - normal cornea (1 irritated, 2 unirritated eyes).

b) 9 animals - moderate epithelial and superficial stroma keratitis, confined to peripheral cornea (5 irritated, 4 unirritated eyes).

c) Conclusion: findings not severe or unusual for test conditions.

Oxygen Uptake: Generally increased (falling within range for hard and soft contact lenses).

8) Conclusion:

Continuous wear ocular irritation study performed in rabbits showed effects ranging from a minimum to short term reaction for normal eyes to moderate or severe reaction for eyes irritated with Ivory Soap. Rxns. were of types normally seen for rabbits wearing gel contact lenses under experimental test conditions.

F. Toxicity Associated with Concomitant Administration of Ophthalmic Medication:

1) Lab. Performing Study: Barnes Hindes Pharm.
Glen Cureton, Ph.D.
Sunnyvale, California

2) Item tested:

Hydrocurve^{tm} II lenses with the following ophthalmic medications:

a) Digest

b) Visine

c) Clear/Eyes

3) No. of Animals/Group: 2

4) Species: NZW rabbits

5) Parameters Evaluated:

Irritation of cornea, iris and conjunctiva.

6) Results:

All eyes showed mild erythema and vessel injection of sclera and nictitating membranes; injection increased

during wearing period; vasoconstriction occurred when solution was applied.

a) Digest and Clear/Eyes: No epithelial irritation.

b) Visine: Light scattered staining was present in eyes treated with Visine; strippling was mild and was negative at 24 hours.

7) Conclusion:

Ocular decongestants considered relatively safe when applied to rabbit eyes wearing Hydrocurve II contact lens.

F. Primary Ocular Irritation (Lens Extract): NFX111 Eye Irritation and Acute Systemic Toxicity Tests:

1. Lab. Performing Study: Applied Biological Sciences Lab. Glendale, California

2. Item Tested: Hydrocurve™ plastic (extracts) in normal saline and cottonseed oil.

3. Regimen:

a. Systemic Assay: 50 mg/kg IV, 50 ml/kg IP

b. Eye Irritation: 72-hour single dose; 0.2 ml instilled per eye.

4. Species:

a. Systemic Assay: mouse

b. Eye Irritation: rabbit

5. Results: No significant irritation observed.

II. Evaluation:

A. Preclinical studies done with Hydrocurve™ (subject of approved NDA 17-367) and Hydrocurve (Hedfilcon A, the subject of the present submission) support the safe use of Hydrocurve (Hedfilcon A) contact lens in man.

III. Recommendation:

Approval of NDA 17-752 for Hydrocurve (Hedfilcon A).

Norma Browder

Norma J. Browder, Ph
Division of Anti-Inf
Drug Products

cc:
Orig. NDA
HFD-108
HFD-140
HFD-140/CSO
HFD-140/NJBrowder:lb/2-16-77

mtg 2/16/77

NDA 17-752
Soft Lenses, Inc.

February 12, 1977

MICROBIOLOGIST'S REVIEW OF NDA 17-752

Name of Drug

Hydrocure (Hedfilcon A) hydrophilic contact lens.

This is an NDA for a lens which is the same as the marketed Hydrocurve Lens but the polymer is produced by Soft Lenses, Inc. This lens appears to have a lower rejection rate for buttons and probably is a more highly purified material.

I. Sterilization of Lenses

This lens is steam sterilized. Spore strips are used in the sterilization.

The USP testing was reviewed and found to be incorrect in the culturing procedures and the number of lenses tested. The numbers and techniques have been altered and are now acceptable.

II. Lens Care and Disinfection Procedures

Both heat and cold chemical disinfection were submitted for this lens.

1. Heat disinfection. This procedure is the same as approved for the Hydrocurve lens. The microbiological testing with Boil N Soak as the preserved saline solution for disinfection was performed by Burton Parsons. A twenty-item type test was performed with two organisms and both were negative. The precleaners to be used with this lens are Preflex and SoftMate. Both cleaners have been tested for preservative effectiveness according to the revised microbiological guidelines and are approvable.

2. The twenty-item test was also run with the chemical disinfection system with two resistant organisms and it was also negative and is

approvable. All of these solutions are sold in multiple-use containers and the preservative test with organic load and a rechallenge as described in the revised microbiological guidelines.

Both heat disinfection with the Hydrotherm II, adjunctive cleaner(s), preserved saline and chemical disinfection with Preflex, Flexol and Normol are approvable with this lens.

III. Cul-de-sac Culturing/Lens Case Culturing

A series of patients were followed for varying sampling times. Adequate numbers were followed for 5 months and some for 6 months.

The procedures were reviewed and are acceptable. Both the cul-de-sac results and those with cases gave results consistent with no alteration in the normal flora.

The organisms frequently isolated from the cul-de-sac were primarily Staphylococcus epidermidis, Cornybacterium xerosum and Propionibacterium acnes, which constitute the normal skin flora. Occasionally isolates of Streptococcus, Candida, Enterobacter or Bacillus were seen. None of these persisted and often were not seen in the case cultures.

As a conclusion, it can be said that the wearing of lenses made from Hedfilcon did not alter the normal flora of the cul-de-sac and that in use the disinfection system did not allow significant cross-contamination of the lens, lens case and cul-de-sac.

This application is approvable on the basis of the microbiology data submitted.

Mary K. Bruch

cc:
Orig NDA
HFD-108
HFD-140
HFD-140/CSO
HFD-140/MKBruch:
11b-2/24/77

SUMMARY FOR BASIS OF APPROVAL

NDA 17-752

Drug Generic Name: Bufilcon A

Applicant: Soft Lenses, Inc.
8006 Engineer Road
San Diego, California 92111

Drug Trade Name: HydroCurve II Hydrophilic Contact Lens

I. Indications for use:

HydroCurve II Contact Lenses PHP are indicated for the correction of visual acuity in persons with nondiseased eyes who have spherical ametropias; refractive astigmatism of 1.50 diopters or less and/or corneal astigmatism of 2.00 diopters or less and aphakia.

II. Dosage form, route of administration and recommended dosage.

Each lens is supplied sterile in a glass vial containing normal saline solution. They are applied topically to the eye and are to be worn all working hours.

III. Manufacturing and Controls:

A. Manufacturing and Controls: The specifications and test methods for the blanks, unhydrated and hydrated lenses and ancillary materials are adequate. The description of the manufacturing procedure is adequate.

B. Stability Studies: Results of stability studies conducted at room temperature were submitted for lots of the finished lenses. The data supports a 24 months expiration dating.

C. Methods Validation: Methods do not lend themselves to classical methods of validation. Validation is waived.

D. Labeling: The package insert, the container label, the instructions manual, the fitting guide and the solution labels are satisfactory as to the format.

E. Establishment Inspection: Memo dated February 7, 1977 from David Bryant states that firm is in compliance with Current Good Manufacturing Practice Regulations with the exception of sterility

testing of the finished product. The firm has corrected this in their submission dated February 7, 1977 (Firm will sample and test product according to USP XIX).

F. Environmental Impact Analysis Report (EIAR): An environment impact analysis report indicates that an environmental impact statement is not necessary.

IV. Pharmacology:

A. Preclinical studies done to date with HydroCurve bufilcon A) have been performed according to our guidelines for toxicological testing of new contact lenses and soaking/wetting solutions used with new contact lenses.

B. Preclinical studies done to date with HydroCurve support the safe use of HydroCurve bufilcon A) Contact Lens and ancillary products proposed for use with HydroCurve in man.

V. Microbiology:

Microbiological testing to meet the current Guidelines for testing of new contact lenses have been performed. Two methods of disinfection are approvable. Heat disinfection with sterile preserved saline in the Hydrotherm II Unit after the use of one of two labeled precleaners and chemical disinfection with the Burton Parsons Preflex, Flexol and Normol regimen are approvable.

Cul-de-sac cultures were performed on an adequate number of patients and there was no change in the normal flora of the cul-de-sac.

Adequate procedures for initial finished product sterilization and testing have been instituted by the sponsor.

The final printed labeling has been reviewed particularly with reference to the disinfection procedures and it is approvable.

VI. Medical:

The bufilcon A hydrophilic contact lens is being substituted for the hefilcon A contact lens. The material is manufactured by the sponsor

and is essentially physically identical and chemically indistinguishable from the material now being used for HydroCurve Contact Lenses.

The sponsor has included a total of 458 patients in this study. Clinical studies presented in this NDA were carried out by 12 investigators:

M. J. Berman, M.D.
Perry Binder, M.D. 294-6244
James R. Householder, M.D.
Harold L. Sabre, O.D.
Harry C. Smith, O.D.
Denton L. Kimball, O.D.
A. Harry Malin, O.D.
Dale A. Rorabough, O.D.
Leroy Rhein, M.D. 286-3711
James S. Russell, M.D.
John Kohler, O.D.
Max Smith, M.D.

314
104

The age range of the patients was 13 to 64 years. The visual acuity obtained by 429 of the patients was 20/30 or better. This meets the current requirements of the FDA Clinical Guidelines. A total of 252 patients wore their lenses for twelve hours or longer.

There were 26 patients discontinued during the study. Seventeen of these patients did not have satisfactory visual acuity, four patients were uncomfortable, one patient had a handling problem and no reason for discontinuation was given for three patients.

There were no adverse reactions reported in this study. Slit lamp findings were unique in that by the third follow-up visit there were only two cases of infection and two cases of edema. There was no iritis or vascularization reported.

Disinfection can be either by the heat or chemical method.

VII. Package Insert Attached.

cc:
Orig. NDA
HFD-140
HFD-140/CSO
HFD-108
HFD-140/ARCasola
HFD-140/NJBrowder
HFD-140/JMDavitt
HFD-140/MKBruch
HFD-140/Scafidi:mef/3-3-77

CONTINUOUS CURVE
RESUBMISSION
NDA ORIG AMENDMENT

JUNE 7, 1976

AMENDMENT 1
NDA 17-752

RECEIVED
JUN 8 1976
HFD-140
BUREAU OF DRUGS

MERLE GIBSON, M.D.
DIVISION DIRECTOR
DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS
BUREAU OF DRUGS
FOOD AND DRUG ADMINISTRATION
5600 FISHERS LANE
ROCKVILLE, MARYLAND 20852

DEAR DR. GIBSON:

REFERENCE IS MADE TO NDA 17-752, DATED JULY 11, 1975.

REFERENCE IS ALSO MADE TO THE LETTER FROM DR. MARION J. FINKEL, DATED FEBRUARY 19, 1976, STATING THAT THE APPLICATION WAS NOT APPROVABLE BECAUSE THERE WERE NOT SUFFICIENT PATIENTS IN THE CLINICAL PORTION OF THE APPLICATION, AND A COMPLETE REVIEW OF THE OTHER ASPECTS OF THE APPLICATION WOULD BE HELD IN ABEYANCE UNTIL ADDITIONAL AND ADEQUATE CLINICAL DATA HAD BEEN RECEIVED.

SPECIFIC REFERENCE IS ALSO MADE TO THE COVER LETTER OF THE JULY 11 SUBMISSION IN TWO RESPECTS:

1. THE FINAL USAN (UNITED STATES ADOPTED NAMES COUNCIL) NAME OF THE MATERIAL IS "BUFILCON A" INSTEAD OF THE TENTATIVE NAME "HEDFILCON A" AS STATED IN THE INITIAL COVER LETTER. (DOCUMENTATION OF THE NAME "BUFILCON A" IS INCLUDED IN THIS AMENDMENT, UNDER SECTION 2c.)

2. THE REASONS FOR THE URGENCY OF THIS NDA AND THE REQUEST FOR PROMPT REVIEWAL REMAIN THE SAME.

THIS AMENDMENT CONTAINS, IN ADDITION TO THE CLINICAL DATA, THE COMPLETE PROCEDURES FOR THE MANUFACTURE OF BUFILCON A. THIS MATERIAL IS NOW BEING FABRICATED BY SOFT LENSES, INC., SAN DIEGO, CALIFORNIA, INSTEAD OF BURTON, PARSONS & CO., INC., WASHINGTON, D.C. DOCUMENTATION SHOWING THE COMPLETE CHEMICAL AND PHYSICAL EQUIVALENCY OF BUFILCON A MANUFACTURED BY BURTON, PARSONS & CO., INC., AND SOFT LENSES, INC., IS ALSO INCLUDED.

AGAIN, WE REQUEST YOUR PROMPT ATTENTION TO THIS APPLICATION.

SINCERELY YOURS,

Donald Brucker

DONALD BRUCKER, O.D.
PRESIDENT

[Whereupon, at 12:40 p.m., the subcommittee was adjourned.]

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