UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

| | |
|---|---|
| IN RE: FRESENIUS GRANUFLO/ NATURALYTE DIALYSATE PRODUCTS LIABILITY LITIGATION | No. 1:13-md-02428-DPW |

BEFORE: THE HONORABLE DOUGLAS P. WOODLOCK
UNITED STATES DISTRICT COURT JUDGE

- AND -

THE HONORABLE MAYNARD M. KIRPALANI
MASSACHUSETTS SUPERIOR COURT JUDGE
SUFFOLK COUNTY SUPERIOR COURT - CASE NO. 13-CV-3400

DAY THREE OF DAUBERT HEARING

John Joseph Moakley United States Courthouse
Courtroom No. 1
One Courthouse Way
Boston, MA 02210
Thursday, November 19, 2015
9:10 a.m.

Brenda K. Hancock, RMR, CRR
Official Court Reporter
John Joseph Moakley United States Courthouse
One Courthouse Way
Boston, MA 02210
(617)439-3214

APPEARANCES:

ON BEHALF OF PLAINTIFFS:

KREINDLER & KREINDLER
By: Anthony Tarricone, Esq.
277 Dartmouth Street
Boston, MA 02116

JANET, JENNER & SUGGS, LLC
By: Brian Ketterer, Esq.
Justin Browne, Esq.
Commerce Centre East
1777 Reisterstown Road, Suite 165
Baltimore, MD 21208

SUGARMAN, ROGERS, BARSHAK & COHEN
By: Michael S. Appel, Esq.
101 Merrimac Street
Boston, MA 02114-4737

ON BEHALF OF DEFENDANTS:

COLLORA LLP
By: William H. Kettlewell, Esq.
Maria Durant, Esq.
100 High Street
20th Floor
Boston, MA 02110

FISH & RICHARDSON P.C.
By: Juanita R. Brooks, Esq.
Thomas M. Melsheimer, Esq.
Roger A. Denning, Esq.
12390 El Camino Real
San Diego, CA 92130

DOWD BENNETT LLP
By: James F. Bennett, Esq.
7733 Forsyth Blvd.
Suite 1900
St. Louis, MO 63105

ALSO PRESENT:
Ronald Castle, Esq.
Fresenius

(The following proceedings were held in open court before the Honorable Douglas P. Woodlock, United States District Judge, United States District Court, District of Massachusetts, at the John J. Moakley United States Courthouse, One Courthouse Way, Courtroom 1, Boston, Massachusetts, on Thursday, November 19, 2014):

THE CLERK: All rise. This is MDL-13-02428, In Re: Fresenius GranuFlo Litigation. Court is in session. You may be seated.

JUDGE WOODLOCK: Well, from our perspectives together, we wanted to explore a bit further the Colton and Zydney matters in light of the back and forth, but also in light of Judge Kirpalani's Memorandum and Order with respect to Daubert matters. As I emphasized, of course, we will separately make our own determinations about that, but I do not see any real daylight between the treatment in Judge Kirpalani's Memorandum and the way I am likely to treat both Dr. Lipps and Dr. Maddux.

I start with that by emphasizing that the state of the play, at least in the initial briefing regarding Colton and Zydney, was that Colton and Zydney were offered to rebut Lipps, and nobody has challenged Sargent. So, I guess it is important for us to know what the views of the parties are about Colton and Zydney at this point. Have they taken on a life of their own now, and, if so, how are we going to address it?

I certainly would not hold someone to their initial

strategic judgment about attacking Lipps with Colton and Zydney. Now Lipps has been somewhat contained by Judge Kirpalani's decision, which, as I have indicated, I think will be coincident with mine. But maybe a way of talking about it or understanding it is to understand how you plan on playing out with Colton and Zydney and Sargent.

So, having framed it in that fashion, maybe you can respond.

MR. KETTERER: Of course, your Honor.

Good morning, your Honors. Brian Ketterer on behalf of the plaintiffs.

So, with that understanding in mind, your Honor, let me sort of come at where the plaintiffs sit with this. The purpose that you framed or that you set up with respect to what the purpose of Colton and Zydney were initially is partially accurate in the sense that there was a historical development of the overall theory that is a centerpiece of the defense, which is this idea that the delimiter is very important and, as a result of having this delimiter, that you cannot exceed the dialysate or the prescribed bicarbonate. I don't know that that's necessarily so key to the plaintiffs' theory.

But one of the other issues that, of course, the defendant takes issue with is how much acetate actually transfers over from GranuFlo and how much of that acetate metabolizes to bicarbonate. One of the things that they have

espoused over and over again, which is a difference between the parties, is that, well, the amount of bicarbonate that transfers over is not a 1-to-1 ratio, meaning that for every 8 milliequivalents per liter of acetate that does not necessarily equal 8 milliequivalents of bicarbonate that's metabolized in the patient; that there is a metabolization rate, and only some of that will actually metabolize and add or contribute to the bicarbonate value. From that standpoint, the plaintiffs don't necessarily disagree with that basic construct. Not all 8 milliequivalents of acetate are going to transfer over and metabolize into bicarbonate.

JUDGE WOODLOCK: Not, again, to hold you entirely to it, but the Master Complaint makes it a little bit like simple arithmetic.

MR. KETTERER: And I agree with that, your Honor, and I guess what I would say with respect to the Master Complaint in terms of simple arithmetic, what is being expressed there is what is the total available buffer source. So, unfortunately, the Clerk had asked me would I like a flip chart. I probably should have said, "Yes," now that I'm thinking about it, but the arithmetic formula that I drew up on the board and that we saw last time in the last hearing, your Honor, was there is an expression. Now, the expression that's up there is no different than what Dr. Lazarus or Dr. Maddux testified at their deposition to. What they take issue with is you cannot

add 35 and 8 and say, well, there's 43 milliequivalents of bicarbonate that is in the patient's blood. If that were the argument, that would be inaccurate.

What we're arguing is that there are two sources of buffer that are available to be delivered to the patient. There's a bicarbonate contribution. That's the 35. That's dialysate bicarbonate. And there's an acetate which will convert in the liver at some rate to bicarbonate. The 35 plus 8 is simply saying this is the total buffer that is available to be delivered to the patient. There's no disagreement, at least from Dr. Lazarus or Dr. Maddux, that that is accurate in the sense of that's available. Now, the issue is how much of that 8 which hasn't been accounted for -- there was at least confusion. That's the factual dispute, what's the level of the confusion and how much of it is being accounted for or not accounted for, which is a question of fact individual to each case, but whether it's being accounted for accurately, and then how much of it moves over, and is the movement over of that bicarbonate, therefore, meaningful.

And the reason why I am explaining all of this, your Honor, not just in answering your question, but it is the foundation behind the very reason why we're here about Colton and Zydney specifically.

So, if the question is these are the two available sources of buffer and the acetate, which is the product at

issue in this case, GranuFlo, moves over at some rate and it contributes to some level of the serum bicarbonate, the question is as a matter of proof what's the amount that moves over, and is that meaningful to the patient? So, there's an actual question in terms of the physical or chemical properties and then a clinical question as to what the meaning is.

Now, a lot of the discussion we had at the last Daubert hearing centered around the clinical meanings, and we have rulings from Judge Kirpalani in the state court matter as to what's going to come in or what isn't going to come in and the sources of data and what we're going to consider there. Another piece is this issue of what's the rate of how it moves over? And that's one of the questions that is -- that's what started Dr. Lipps on looking at some of the questions. They were looking at how much of this acetate really moves over, is it really meaningful? Now, as your Honor noted, he has been contained in terms of moving, about acetate transport issues, and I would argue that Mr. Sargent or Dr. Sargent is essentially saying a response or a rebuttal to Colton and Zydney, so the only way Sargent comes in is if Colton and Zydney come in. But the reason why --

JUDGE WOODLOCK: Let me just stop you on this.

MR. KETTERER: Sorry.

JUDGE WOODLOCK: This is, again, strategic.

MR. KETTERER: Sure.

JUDGE WOODLOCK: It is just so I can understand the state of the play. Assume we say, or one of us says, that Colton and Zydney are out and Sargent is out. Now, if Colton and Zydney are out are you dead in the water?

MR. KETTERER: No, we're not dead in the water, your Honor, because the synthesis of the data can occur through other general causation experts, especially from the plaintiffs' point of view. What I would say about the rate of acetate transport, specifically about how much moves over, one of the reasons we have this vacuum of data is that it has not been a studied issue beyond acetate-only dialysis and the modeling that Colton and Zydney did about the specific subject.

The ABCDH (sic) Study, your Honor --

(Pause)

MR. KETTERER: Sorry. My mouth was dry again. I apologize, your Honor.

So, the Colton and Zydney information talks about or fills in a gap that is vacant from the literature to some degree and the fact that the company itself hasn't studied the issue.

JUDGE WOODLOCK: Let me pause on that, because I want to be sure that there is not a suggestion that there is going to be in Colton's testimony, if he testifies, the kind of feistiness about discovery that suffused some of his answers that suggested that the reason that there was not the study is

that they were afraid of what the study was going be to, which seems to me to be beyond his competence. It may illustrate his partisanship but not his competence on the issue of expertise.

MR. KETTERER: If the suggestion, your Honor, is that the Court would frown upon the idea of imputing a thought as to why the defendant -- or a motive to the defendant, I would agree with you, that that would be improper for him to offer that in the --

JUDGE WOODLOCK: So, he testifies that there was limited, "he," meaning Colton or Zydney, because I gather they are like Cheech and Chong --

MR. KETTERER: One or the other.

JUDGE WOODLOCK: -- one or the other will show up at a given time?

MR. KETTERER: One or the other.

JUDGE WOODLOCK: The testimony will be, if I am correct, is there is not a lot of data for a variety of reasons. Some of it is old. There is some newer data. Here is the ABC -- I will not go any farther with it --

MR. KETTERER: DH (sic).

JUDGE WOODLOCK: -- and that is the thrust of what they are going to say?

MR. KETTERER: Two instances, your Honor. One, they talk about the VFX data, which is something that we talked about, in their modeling. They would also discuss the

ABCDH (sic) I think in part because it's important to analyze all the data. It's certainly something that I would expect the defendants to cross him on, because I think that they would question, and they have, indeed, in this particular argument, that they've questioned the validity of the modeling based on the results of the ABCDH (sic). The question of modeling or what they would say in response to that is some of the fact of what are the problems with how the ABCDH (sic) was constructed and how the patients were selected.

Now, one of the interesting things is that FMC controlled the selection of all the patients. It's an FMC clinic. They have controlled the parameters of the data, and I would be happy to supplement this. If you read the deposition of William Smith, who was the principal investigator on the ABCDH (sic) Study, he testified to this. Although he was independent, he didn't do any of the selection. He didn't control what patients were going to be part of the study and which were going to be excluded. So, one of the things of the observations that Dr. Colton and Zydney made in their report is, look, when you are looking for an explanation as to why there may not be the same replication of the accuracy of the modeling to the result, some of it may have to do with the patients. It's also a small sample size. There's six to ten patients, really six that were a valid part, as per Dr. Smith, that were really valid data that were results from

that particular study.

So, the question of what they're going to come in and say, to get back to the question you asked, is, they are going to talk about what was the predicted rate, and they are not writing -- I think it would be a bad move for a trial lawyer to come in and say, and put up a mathematical equation before the jury. We are not trying to bedazzle the jury, and I don't know that you would bedazzle the jury with some long, complex equation in multiple format. I think that would be a waste of time, and that's not the plan.

But the foundation behind the analysis and the foundation behind how they got the results of what they are predicting the amount of acetate that's moving over and what converts to bicarbonate, that is what the purpose of the modeling and the analysis of both the VFX and the ABCDH (sic) Study to be, and that's what they're testifying about. And I think that that's important data and important information when the centralized dispute is, your Honor, that the question of GranuFlo works in this fashion. One of their defenses is the contribution isn't meaningful, therefore, the plaintiffs should have the opportunity to present the evidence to say, "This is how much moves over."

Now, as a clinical issue, another physician is going to come in and say, "Look, this is the clinical aspect." They are not physicians, they are not medical doctors, so they can't

testify and say, "This is the clinical impact on the patient." That's for someone else. But when we are talking about this in the abstract, if you are going to get up and cross the doctor or any of the general causation people or any of the causation people and say, "Well, how do you know whether the acetate contribution was significant, or what are you pointing to or what are you alleging is really significant about this acetate moving over?", I think it's important to know and to have testimony about this that says, "Look, not only do we have the modeling. Now we have actual patient data to look at, and we have actual patient data to predict what the rate of metabolism is going to be and how much that is going to contribute to the overall bicarbonate load."

I think that that's a central part and an answer to the question.

JUDGE WOODLOCK: So, let's treat this in two parts. The first part is, yes, this form of equation is used in making analysis of issues like this in pharma, but that is at a pretty high level of generality to say that, and the challenge to that is that there are too many variables here that are just inadequately developed, and to some degree there is a subtheme in your analysis as well that says, "Yes, there are. That is Fresenius's fault, but, yes, there are these problems, but we have a scientific methodology that is acceptable, or at least used by people, but it is really the fit that is important.

And so we look at the data that is there and what they have done with it, and the suggestion is that they have not fairly analyzed closely the ABCDH (sic) results. We have gotten down into the weeds with each of the individual patients on it." So, what is the response to that, just so let them cross-examine about that and see what happens?

MR. KETTERER: I think to some degree the answer is that cross-examination fetters (ph) out what exactly is the problem in the analysis if, your Honor, there weren't other data that did validate the model, and I would argue that ABCDH (sic) did not invalidate the model, and I think that when you look at the parameters --

JUDGE WOODLOCK: But hasn't it become a kind of force-fit when you look at the way in which they -- finally they got it. They were the dog that chased the car. Then they caught the car. Now what are they supposed to do with it? And what they did with it was force fit their previous analysis to meet the constraints that they had from their model.

MR. KETTERER: Well, your Honor, I guess my response to that line of fact would be you would be correct in criticizing it for that reason if they had had the benefit of saying, "Well, I had this data before I even started constructing my model, and then I went back and tried to -- and then I built my model and then tried to go back and work the data back in." But that's not the way it happened, though.

JUDGE WOODLOCK: And the chronology, that is an important point, I think, which is to say it should be where things stand at the time of trial. There is always fun to be had about how someone got to a particular position, but I raise it simply to force the issue for us. The question, I think, would be, "All right. Now I have got what I have got." This is Colton or Zydney. "I have got what I have got. I am prepared to testify. I stand behind this modeling."

MR. KETTERER: Well, there's another way to approach the testimony, your Honor.

JUDGE WOODLOCK: All right.

MR. KETTERER: And one of the other ways to approach the testimony is to say, "Did you analyze patient data? Did you get data from VFX and did you analyze what the rate of metabolism is?"

So, for instance -- we have been very model-focused here, and I don't know -- again, please don't hold me to this in the way that -- because I don't want to argue to you that the model is invalid. I'm not agreeing to that. But, as a matter of practicality, how might we present this information? Well, we might present it as an analysis of actual patient data rather than a model that is then validated or invalidated or whatever else through patient data.

So, for instance, what I mean by that is the discussion that, let's say, Dr. Colton or Zydney would have,

is, "This is the data that we were presented. We analyzed the data of these hemodialysis patients. Based on the available data that we had, this was the rate of acetate that was predicted or that we saw in these patients. This was the amount of bicarbonate. Now, is this going to hold true in every single -- and how did we do that? Well, we figured it out. There was a mathematical expression to figure out what that rate was in putting all these different variables, and this was the end result of what we came at."

And what does that tell us? Well, they don't testify about what the clinical impact is, and they can't, obviously, say this is true for every single patient, because every patient has different physiology, but what they can say about it is, certainly from a generalized standpoint they are able to testify, "This is a good predictor of how acetate does react in many patients, and you could change some of those variables and modify it, but there is a range at which it would go, based on what we've analyzed."

And that's certainly another way of coming at this idea of, and what I take to be, some of your Honor's question to be, is, "Look, you have this model. The methodology of modeling might be sound, but the methodology of modeling for this particular variable is not something which is replete throughout the literature. So, what's your foundation for the methodology being sound on this particular point?" Part of my

answer is, well, it's modeling that they do at FMC and have done on acetate prediction, and that's what they asked Frank Gotch to do, which we will be talking about later with Judge Kirpalani. But that's what they asked Dr. Gotch to do. So, they are sort of coming in and saying, "Well, the modeling is invalid. Dr. Lipps did some of that modeling. Well, they were going to exclude that, but then Dr. Gotch did some of that modeling. That was some of the basis for how the entire story started, and now we want to complain about that methodology."

Now, you say, "Well, look, let's forget about that. Let's fast forward to what we have here and now today. If you set the modeling aside and you actually looked at patient data, what's the value in referencing back to the modeling per se?" And I guess my response on this point is, look, the modeling is important because, one, it's developmental. It's part of how we got to the point we got to of why they're here and what the value is in predicting it. I think that if one set of data which is larger and has more patients is accurately fitting the model, that's as much to consider as saying, "Well, I have this other set of data that I am going to admit up front is not as much of a match as the VFX," but that doesn't invalidate the modeling. No modeling is perfect.

They use Kt over V, which is basically to look at urea clearance, and that modeling has been used and it is used as a measure of clinical practice every single day. But whether or

not that works for every single patient and their different physiology and whether it's accurate is all over the map. That's why there's a controversy about always using it. Now, they've accepted it. It's accepted in nephrology practice.

But to say that there's no validity or no sound methodology behind the modeling, I don't think that that's accurate or fair either based on the entirety of the look. But, again, if we are talking about what the practical implication is of how this would be presented, I think my suggestion of we're going to look at the patient data first because that's the most important thing to analyze first, I do think that that's probably, assuming that your Honor's ruling allows for it, that is the way we might have approached it regardless; that it is not a lead-in with the model that we are so concerned about or that I am concerned about.

I would much rather have -- and I think that if Drs. Colton or Zydney were asked about this or were to come in and tell you this, they would say the same thing, they would rather have the actual patient data up front. But we didn't have that. We didn't get that VFX data, that, even though it was three years old, we didn't get that. The ABCDH (sic) Study wasn't finished until, and as your Honors are both aware, until September of 2015.

JUDGE WOODLOCK: But what does that mean? Are you saying that they cannot do the patient data?

MR. KETTERER: I'm saying that it wasn't made available --

JUDGE WOODLOCK: I will concede that for the moment. So what?

MR. KETTERER: Well, I think that what it helps to do is it helps -- I want to make sure. I'm not 100 percent sure when you say, "So what?", what you want me to respond to on that.

JUDGE WOODLOCK: Well, if you say, "Here is how it is going to play out: It is not going to be about modeling, it is going to be about data, patient data." You have got all there is, I guess, or at least all that is going to come out before trial.

MR. KETTERER: Right.

JUDGE WOODLOCK: Are they restyling their opinion, then --

MR. KETTERER: No.

JUDGE WOODLOCK: -- or, based on the opinions that they have, they simply lead with the patient data?

MR. KETTERER: Right. And I think that what they would say is, "Look, this is the rate of acetate that we expected based on the analysis. This is what actually metabolized and here is how much would go over to bicarbonate," and some of that is based on predicting, some of it is based on what they actually saw. And the only part of the prediction,

your Honor, becomes how does that extrapolate out based on what we see for a larger volume of patients, right?

I guess, you know, I don't want to go over and over this point, because I know you get it, but I do think it's important to note that the whole reason that we have this kind of analysis or we're in this position is because the data doesn't exist about how the product actually works outside of Colton and Zydney doing the work. That is sort of a fundamental wedge that I am in as a plaintiff. It is not like you can tell me, "Well, go to the literature, go to the textbook and use that instead." I don't have the benefit of that. And I can't go to the company data, because they don't have it either. They don't actually understand how much is -- now they do. Because of the litigation they have started looking at it, but prior to that they didn't look at it.

So, I had to hire experts, or we've had to hire experts, to analyze this question, look at the available data that was there, run it based on all the parameters that they needed to in order to reasonably consider it so they wouldn't be criticized for not considering these other portions of the actual analysis in the data, and before they had that they ran a model in order to answer that same question, because the only data that they had was based on acetate-only dialysis. Those were the patient parameters, and the defendant criticized them for using -- despite Mr. Lipps doing the same thing, they

criticized them for using only acetate-only literature in the parameters.

So, now we have something else. We have other data to look at. That's why I said I would prefer to lead with the data. But it doesn't invalidate the purpose or the utility of the actual modeling, and I think that that's --

JUDGE WOODLOCK: I guess it does if the model is out of sync with the data itself, or if the model is contorted. I do not mean that in a chronological sense but simply that here we have got the data, and here we have got the model, and the model is making certain assumptions that it is done kind of backdoor.

MR. KETTERER: I guess the issue that I would take with it is that I don't think it's backdoor fitting, your Honor. I think that there are -- number one, I think that you can't focus only on the ABCDH (sic) and say, okay, in ABCDH (sic) it didn't exactly fit. Well, that's six patients, and I agree that, first of all, one it did, and on the others it didn't, and there are issues behind that. There are issues behind what kinds of patients were selected to be part of that study, what are the reasons why it may or may not fit. Those are the kinds of questions for cross-examination. And if they only base the modeling and the only data we had was the ABCDH (sic), your Honor, I think the argument about "square peg, round hole" would probably be more analogous and fair. But I

don't think that what they are doing is, is trying to backdoor it. I think that they have basically said up front, "Look, it's not as much of a fit as VFX." But if we only focused on the one set of data, then I think there is something to this idea of, "Are you just trying to make something fit that doesn't fit?" That's not the case. So, we can't forget about the first half of their analysis and of the data.

And that's the reason why, I think, your Honor, when you talk about the modeling and putting it in as a portion of cross, to the extent that modeling is really brought up as a significant basis, that that's a portion for cross-examination to say, "Look, you ran it against two, and in one your model wasn't as accurate a fit as it was on this other data." But if we're saying, like, "We have this data set of 6 patients but we have this other data set of 16 patients," it's not simply by virtue of the fact that you have more numbers that it makes it more valid, but I do think you have more results when you consider the data to say, "I have more results to look at to see whether the model was accurate or inaccurate."

Or, to put it another way, your Honor, if you added the two results together and said, "Based on a percentage how often do the model -- was the model accurate?" Well, the fact that you had 16 patients and it more accurately predicted among those 16 patients would certainly raise the average of the percentage of the accuracy.

And I'm not suggesting that that's the correct way to approach it from an analytics standpoint. What I'm simply suggesting is that, when you look at this one set of data, the ABCDH (sic), the importance of looking at it is, of course, that it's important data to consider, but it's not standing alone; it's not an analysis which exists in a vacuum. It's an analysis which is part of another analysis, which is part of a model that was constructed, and the modeling has value and benefit if it expresses and if it accurately reflects both portions of data.

In some ways it accurately reflects ABCDH (sic), but no model is ever going to be perfect, whether computer models, whether models for dialysis, models in any sort of discipline. There is no such thing as a model which perfectly and accurately predicts every scenario. And I think that, I'm sure you have had experience with engineering cases, and that's true, and yet for methodological purposes, for Daubert purposes, modeling is still an accepted methodology, and I think that, even more specifically, modeling in nephrology and in nephrology practice is used.

JUDGE WOODLOCK: Well, I wanted to hear, obviously, from the defendants on that. I do not know if Judge Kirpalani has any further questions of you.

JUDGE KIRPALANI: No. I think Judge Woodlock has articulated all the questions I had for the plaintiffs.

JUDGE WOODLOCK: This is perhaps more a federal question or maybe First Circuit question, but after Millward One, and as we wait for Millward Two, isn't this cross-examination stuff?

MR. DENNING: So, there is juicy cross-examination material here for Colton and Zydney, particularly based on how their model doesn't fit the actual data. The problem is the subject matter. You saw Equations 16 and 17 that they produced on Monday. The subject matter is so far beyond the ken of the average juror that they are not even going to know when points are scored on cross-examination. They're going to be wowed by the math, they're going to be wowed by --

JUDGE WOODLOCK: I do not know if that is the case. Number one, this is not a 403 case on this, I think, and I think Judge Kirpalani dealt with it with Maddux in the same way. Jurors, focused, can get to these kinds of questions. We cannot say that they cannot. That is what they are there for. They make the decision. We do not just take something away from them because it is challenging.

So, then I am back to the idea of, okay, you have got Dr. Sargent. Dr. Sargent is not lacking for self-assurance and is likely to be able to hold his own here, and why isn't that, as I say, particularly after Millward One, which weighs on my mind, why isn't that to say to the jury, "Go at it," or say to you, "Go at it," and, "Jury, watch this"?

MR. DENNING: I understand. A couple of things. First of all, I'm not suggesting that, just because it's hard, the jury can't see it. That's not my point. My point is -- first of all, this is so far afield from the central core issue of this case, what happened to Mr. Ogburn. It really, as your Honor said, it has kind of taken on a life of its own. This modeling -- we have the ABChD data. We can look at that. They can have their experts, not Drs. Colton and Zydney, who are chemical engineers, not nephrologists or physicians, but look at the ABChD data and say what that means from a clinical perspective. Of course that's open to them, and that's really what I think the jury should be focused on in this case, is what the actual data is, what happened to Mr. Ogburn, what happened to actual patients, not this model that they dreamed up and that I think is wildly inaccurate as demonstrated by --

JUDGE WOODLOCK: Well, but, to review the travel of the contentions between the parties, it was as a result of Dr. Lipps's epiphany, and, while that has been cabined to some degree in a way, as I said, that I would share, it is going to come in, and it is going to come in that his view is that there is an upward limit, and the upward limit is whatever the dialysate had. So, somebody gets to talk about that.

MR. DENNING: So, I think what Dr. Lipps would say and what our experts have said is that if -- they are not saying it never goes above the level of bicarbonate in the dialysate.

That's not what they're saying. They are saying if it does go above, then it starts to diffuse back into the dialysate. So, it can get a little bit above, the serum bicarbonate can be a little higher than the dialysate bicarbonate, because it takes some time for that reverse concentration gradient to come into effect. I think everybody agrees with that. I don't think that, just like Mr. Ketterer said, that now everybody seems to agree that total buffer isn't actually factual. We agree with that. I think they also agree that the reverse concentration gradient would cause things to flow back. Every one of their experts testified that that's true. So, I don't think that that's a matter of dispute at the trial either.

What they are trying to influx into this is this model that tries to predict, okay, the volume of distribution of bicarbonate in the body, the volume of distribution of acetate in the body, how are those going to intertwine and affect the ultimate levels? That part they got wrong. If you look at their model it's incorrect, and we can critique it on cross, but really it's more of a fundamental flaw in their model that shouldn't even go to the jury. It hasn't been peer reviewed. The testing that they did, the only testing they did shows that it's not reliable. It's not the type of analysis that should go before a jury.

Your Honor, if I could hand up just a few slides on this point?

JUDGE WOODLOCK: Sure.

MR. DENNING: If I can get it to show on the screen here.

So, to kind of recast how we got here, and this is Slide 2 of the slide deck, for the record, last time we were here we pointed out that Drs. Colton and Zydney used dialysance rates that they estimated because they didn't realize that there were actual flow rates shown in the ABChD data. So, they were sent back and said, "Okay, use the actual data. You've overestimated by a factor of two to four the amount of bicarbonate that goes through. Use the actual data and see what happens." That's what they've done. They have gone back and they've refit their model so that they can use the actual data from ABChD.

And this next figure, this is Slide 3, shows kind of the process that they've gone through. They developed this original model, and they developed it with the Mion and Bruno data. That was the acetate-only data from 30 years ago with only three patients. But that's how they developed their model. They then applied it to the VFX and the ABChD studies, and when they did that they decided they had to use a different dialysance for the acetate than they were using for the bicarbonate. They realized it was a mistake in their original model, and to make it fit ABChD and VFX they had to use different dialysance. So, they did, and that was the first

kind of change to the model or patch that they made. Then they realized, well, they used the wrong D Sub A and D Sub B. So, then they had to use the actual flow rates, and that's what they did. When they used the actual flow rates, and this is what has happened since the last time we were together, their data didn't fit the model at all, not even close. They realized, "Oh, well, now we need to, to fit the ABChD Study, take two, we need to add ultrafiltration." So, they added that patch to their model.

What they are doing is constantly trying to patch the model, retrofit it, back-fit it to the data in order to make it fit this set of data, to make it fit the next set of data; but, in actuality, the problem is the model itself is flawed, and no matter how many patches they make the underlying model is flawed.

Even with the fixes that they made, and this is Slide 4, and apparently this isn't an issue of dispute anymore because of what I heard counsel for the plaintiffs say, it doesn't fit the ABChD model at all. This is their own experts, Drs. Colton's and Zydney's analysis of how well the model fits the ABChD Study. They said that five of the treatments were good fits, eight were fair fits, and seven were what they called "low" fits. I guess they didn't want to call them "poor" fits or "bad" fits; they called them "low" fits. But clearly this did not fit it well.

And let's look at what they call "poor" and "good." On Slide 5 you can see in the red dots on the left the actual patient data, and the red line is Drs. Colton's and Zydney's model, estimate. It has over-marked it by a factor of 5, 6 milliequivalents per liter. On the right one for Patient 17, again, you can see the Week 1 and Week 2 data in the red circles and the blue triangles, and their estimates of it are 4, 5, 6 milliequivalents per liter over. It's dramatically wrong. And, to their credit, they said, "Yeah, it's a poor fit. Our model doesn't fit this data."

But in the next slide we see what they call the "good" fits. And this is Slide 6. The green dots show the actual patient data. The line shows their model's expectation. But two things are wrong with it. First of all, the slope is entirely different than the slope for the actual data. We can see the actual data plateaus at about 90 minutes into the session, whereas their model doesn't plateau until four hours into the session. That, itself, is a fundamental flaw in the model.

But, second, it again overestimates how much bicarbonate gets into the patient. Here they say it's at roughly 40 or so, whereas in the actual data the last serum bicarbonate level shown is 36. Even in what they call -- this is what they call a "good" fit. So, clearly it doesn't fit the data at all. It's just absolutely wrong.

Well, why is it? A couple of reasons. And Dr. Sargent explains a lot of the flaws in the Colton and Zydney model. One of the fundamental flaws is they treat the volume of distribution of acetate in the body to be the same as the volume of distribution of bicarbonate in the body. They say they're the same, and that's a fundamental characteristic of their model. They've made that assumption. That assumption is wrong.

In Slide 8, and this is testimony from Dr. Goldfarb, plaintiffs' own expert, plaintiffs' nephrologist, who is going to testify in the Ogburn case, I asked him at deposition, I said, "Do you agree...talking about the different volume of distribution of bicarbonate and volume of distribution of acetate, that the volume of distribution of bicarbonate," and the volume of distribution of acetate are different? He said, "Yes, I agree," they're different. Drs. Colton and Zydney have assumed they're the same, and that has permeated their model.

And here is the import of it: If you assume the wrong volume, then you're going to have the wrong concentration, right? "Concentration" is just the amount of bicarbonate or acetate divided by the volume. If you are assuming the wrong volume you are going to end up with the wrong concentration, you are going to end up with too much bicarb going into the system compared to what actually happens. It overestimates the total concentration of bicarb again and again and again.

And in the next slide, Slide 10, this shows how that permeates through all of their equations. These are the two equations that were missing from their supplemental rebuttal and the Court asked them to supply earlier this week, and replete throughout these equations are the concentration gradients C Sub B and C Sub A. Those concentration gradients are wrong because they used the wrong volume of distribution, and then the metabolism rate for acetate, which is the variable R, is also wrong, because, as you can see in Equation C6 at the bottom, that metabolism rate for acetate depends on the concentration of acetate, which is wrong because they used the wrong volume for acetate. So, not only are the C Sub B and C Sub As wrong, but so are the Rs. That's how their model ends up producing results that are dramatically different than reality.

And Dr. Colton admits it. He said -- this is really the ultimate question of reliability and whether a jury should be able to rely on this testimony, this model, when they are deciding this case. In his deposition Dr. Colton said, "Before I would ever advise a nephrologist to rely on the modeling," he means his model, "for prescription, I would want to see data that can be compared with prediction and to assess how good the model is in the framework of how the patients are treated today, and the extent to which there are aberrations."

He said, My model is not ready for prime time, my

model is not ready to be used for prescriptions. If it can't be used for prescriptions, it shouldn't be used by the jury to decide this case.

JUDGE WOODLOCK: I am not sure he said that, what you just said. I am not sure he would say it in the testimony. This is, as you say, juicy for cross-examination.

MR. DENNING: At the very least he said, "I would want to compare it to the data." He has done that since. This deposition was before they did the ABChD. We've now compared it to the data. We didn't get to ask him, "And you agree it doesn't fit, right?" But I think it's pretty apparent from their characterizations of the data that more than 75 percent of them they characterized as not good. I think it's clear he wouldn't call that a good fit. So, ultimately, they admit the model shouldn't be relied upon if it doesn't fit the data. They admit that the model doesn't fit the actual data.

Allowing them to present this model, given really a show of its own, we're talking a significant amount of time in a timed jury trial that the jury is going to be focusing on the model and the equations, which aren't peer reviewed, which aren't accepted in the dialysis community, unlike Kt over V, which, very peer reviewed, accepted, used throughout the nephrology community. This isn't used at all. This has never been used beyond Drs. Colton's and Zydney's reports in this case. To go into that sideshow, particularly given the fact

that this isn't reliable, it's going to be beyond the ken of the jury. Why engage in this sort of sideshow and make us bring Dr. Sargent to counter that?

MR. KETTERER: Your Honor, may I briefly just very quickly respond on this?

JUDGE WOODLOCK: Sure.

MR. KETTERER: And I know you know, you brought it up yourself about Millward, and I don't want to focus on that, I want to go to the substance on that, because my argument about why it is more appropriate for cross is really fundamentally rooted in a substance argument. The idea that the defendants are not arguing the question of how much acetate from GranuFlo reaches the patient is completely incorrect. I mean, they are absolutely arguing about that. That's the central issue, is whether GranuFlo actually causes a rise in bicarbonate, and does a high bicarbonate lead to cardiac arrest? Those are the questions, and it's absolutely relevant in Mr. Ogburn's case as to whether or not that evidence does or doesn't exist.

Counsel asserted some things as if they are facts, but those are actually Dr. Sargent's opinions rather than actual facts, which is the point of whether or not that should be subject for cross-examination because of the fact of he asserts one thing that these constants, that the rate of volume distribution of acetate's the same. Those are opinions of different people. Those are not assertions of fact. So, when

you get up and say something is patently untrue, that's, of course, from his point of view. It's like, you know, Obi-Wan Kenobi saying from a certain point of view that's the way he views the truth. That doesn't actually make it the truth.

The issue is that they focused their entire argument on a six-patient study. That's the other reason. The entire -- and I see your Honor's look, which is that they do mention the VFX, but the critique about the inaccuracy in the data is really focused on ABChD.

JUDGE WOODLOCK: Well, no. That is the most striking one. But there was an argument before, and because I had a little bit more time to work with, with the indulgence of Judge Kirpalani, I said, "Okay, go take a look at it," and you did. It was not very helpful. Not only not very helpful, it was further undermined. So, if I go back to VFX, that was not a perfect match either.

MR. KETTERER: Well, I'm not saying that it was, because, as I said, your Honor, there is no modeling that's going to be a perfect match, and I don't think that's the goal.

JUDGE WOODLOCK: I think the goal is to make it fit as best you can, and it is an iterative process. When people talk about "patches" and that sort of thing, that is the stuff of Ph.D theses. What I am interested in is what does the science say at the time that someone has asked the question, and have they found a fit, and it did not get better for you, it got

worse.

MR. KETTERER: Well, but my point about that is, your Honor, first of all, you are talking about six patients. It didn't get worse. What I would argue is, is that it's another set of data. I think that the construct of looking at it from the standpoint of a linear timeline of, "You looked at this, then you looked at this, and it didn't improve for you," isn't the way that I think that methodologically should --

JUDGE WOODLOCK: That is where we are now. Now you have got a little bit more data, and the little more data is not more helpful, it is less, but the state of it is it is not as strong as it was before. And so I look at it now and say, whatever it was, is it strong enough to permit the jury to think about it?

MR. KETTERER: And I guess that's my sort of answer to it, then you are back to the issue of weight, because what we are doing is, is parsing whether it is good or bad. This idea it's going to be a sideshow, I don't know how much I want to discuss this, but it is not something we plan on presenting three hours of testimony on. This is a short presentation of a witness based, again, primarily on the data, not on the equation. The equation is important -- or the model is important in the sense of the development and what it says about the predicted rate for acetate metabolism generally, which is a central piece of the case.

JUDGE WOODLOCK: The only justification for having Colton and Zydney is that they have a model. There are other witnesses who can testify as to patient data.

MR. KETTERER: Let me just clarify that, your Honor. It's not just the model. They are talking about what the data says about the rate of acetate transport. That is more unique. Although another witness could talk about it, they haven't analyzed the data in the same way, nor are they at the same level of expertise to say, Look, this is not only, not only what the data says, but the VFX required an analysis in order to talk about the rate of acetate metabolism and how much would have -- they input the data into the model in order to be able to make that calculation, but it's just an algorithm which allows them to say, "These are the actual facts of what the acetate metabolization rate is." That is unique to Colton and Zydney.

And so, that expression or discussion of the data from that standpoint is important, but, again, that's my point about why this is not a long presentation. It's not intended to be.

JUDGE WOODLOCK: It may be a long cross.

MR. KETTERER: It could be a long cross, but it's a timed trial, and they're free to use their time however they see fit.

JUDGE WOODLOCK: Well, but then a factor in that, if you want me to start thinking about that as a factor, is, is it

unfair to permit somebody to put in something that they throw out as red herring and have the other side spend their time chasing down the smell or the other sensations that are created by this red herring that is drawn through the courtroom?

MR. KETTERER: I don't know if it would be appropriate or inappropriate, and your Honors have the discretion to make that decision, but what I would disagree with is that it's a red herring, because in this case the fundamental premise of that assumption would be that the evidence presented would be done so for a red herring. Absolutely not. I think, from the plaintiffs' perspective, it's a critical piece of information, a critical data analysis that goes to one of the fundamental critiques that the defendant will jump up in opening and absolutely be talking about. The question of whether their product contributed significantly to the serum bicarbonate such that it would have led to someone becoming alkalemic is, in fact, the central general causation rates, and these witnesses address that.

JUDGE WOODLOCK: I think I understand better than I did before the issues --

MR. KETTERER: Very good, your Honor.

JUDGE WOODLOCK: -- involved here. I have dominated because I am trying to think through this aspect of it. Judge Kirpalani has thought about it much more deeply than I.

MR. KETTERER: And, your Honor, both of you, if you

have any further questions I'm happy to answer anything further along these lines. I do think that I've probably been overly verbose, and I hope that I have addressed the questions.

JUDGE KIRPALANI: So, let me just ask Mr. Denning to focus on the inclusion of the ultrafiltration data in this second go-around, if you will, and why is that problematic to their model? What are they doing, and what is the impact?

MR. DENNING: Sure. What's fundamentally problematic is they did it only for the ABChD data. They didn't do it for the VFX. Why did they do that? Because that's how they could get as close as they could get to ABChD, and if they did it for the VFX, well, then it would make them further away from VFX. That's not a reliable model. If you have to add modules to it for different sets of data so that it more accurately fits that data, then the model is wrong, because they don't know what to add or what not to add if we're talking about patients in general, or if we're talking about Mr. Ogburn, or if we're talking about nephrology patients in the U.S. Are they going to add ultrafiltration to their model for that, like they did for ABChD? Are they not, like they didn't for VFX and for Mion and Bruno?

That's just a fundamental flaw of their model, is, you can't have a model that you have to tweak every time for particular sets of data and then try to say, "Okay, we are going to use this model for everybody or for Mr. Ogburn," when

you don't know the data to compare it against.

MR. KETTERER: I'm sorry, your Honor.

JUDGE KIRPALANI: Yes. Sure.

MR. KETTERER: Look, that's a wholly inaccurate way of portraying the way the modeling works. It's what's the available data and what are the parameters that are input into it that go to what the data or what the model might conclude as a result of running different parameters.

The problem wasn't that they didn't have ultrafiltration. It makes it sound like they didn't consider it. What happened was they didn't -- and this is something that they brought out last time, which your Honor has allowed us to address, which was the ultrafiltration rate was predicted as lower than what the actual information or data they had and then they were able to plug that in. That's not a flaw in the model as if the model failed to consider that fact. The model did consider that fact, but it had an inaccurate parameter in that. The model is not flawed, because the parameters that are contained within the model alter and vary. That is, in fact, what we need to do with patient data.

The reason I come back to Kt over V so often is that it's the same principle of inputting patient data and parameters. That's why that model does not accurately predict clearance in all patients. It's a model. It predicts -- it's physiologically in some patients and not in others. So,

whether it's reliable or unreliable, so on and so forth, that's a separate question. The question is, is that only pronouncing that because some of the data in ABCDH (sic) did not fit the -- some of the runs did not fit the model does not make it wildly inaccurate, it doesn't make it something which is wholly unreliable, because there's other people physiologically who absolutely fit in. So, the question of fact is, or the question on cross isn't to parade them out to say, "Look at this, look at this complex model." It's more to do it as a matter of what do we have to predict how much acetate in patients metabolizes and how much of that becomes bicarbonate, what's the predicted rate? That's the fundamental essence.

JUDGE WOODLOCK: But let me just ask this, so I understand what that means on the ground.

MR. KETTERER: Sure.

JUDGE WOODLOCK: So, we go to Slide 6 of the slides that we were just given, which is, I am told, a good fit. Is that a good fit?

MR. KETTERER: Well, your Honor, again, I would argue that, yes, it is, based on the analysis Drs. Colton and Zydney are offering.

JUDGE WOODLOCK: That is self-referential. If I were looking at something like this for anything would I say, "That is a good fit"?

MR. KETTERER: Well, the answer is, your Honor -- let

me, just from my advantage point, why I would say it's a good fit is that that's a question certainly of fact as to whether or not that is or isn't a good fit, right?

JUDGE WOODLOCK: And that gets to the more fundamental question that I was putting to your friend, which is, what is the gatekeeper role? If it is to be simply a potted palm, I understand that. I do not find it a good fit for me --

(Laughter)

JUDGE WOODLOCK: -- but if that is what I am supposed to do, that is what I am supposed to do. On the other hand, if I am supposed to do something about it, then there is a degree of independent analysis before it gets to the jury, and so I ask the question would a statistician looking at this say that is a pretty good fit?

MR. KETTERER: First of all, I think you would have to ask a statistician on that question.

JUDGE WOODLOCK: Sure.

MR. KETTERER: And I think the most appropriate people to ask would be the experts in this case. That would be Dr. Colton, Dr. Zydney or Dr. Sargent.

JUDGE WOODLOCK: And I think I know what their respective responses would be.

MR. KETTERER: Right. So, they would each have an explanation. So, your Honor, just getting back to your potted-plant analogy, that's the reason why in this instance --

I'm not suggesting, nor am I sort of pronouncing, that in the lexicon of all Daubert hearings that you are to be a potted plant. You are not. Neither Court, in either Lanigan or in Daubert, that's the role of the Court. On the other hand, I think this is the type of situation to which Millward was sort of alluding to, a question where you look at it and the complexities behind are such that you would have to ask the experts in order to explain "good," "bad," "poor," "fair," whatever the issues are about the results from the different studies in the analytics, that that is the kind of question of fact that should be asked to the experts, and that is what Millward is sort of speaking to, in my opinion, of the analysis. It isn't that the Court is somehow completely neutered from making any analysis, nor should it be, and I don't think that there's any Daubert progeny which expects the Court to do so.

But the question is was the methodology sound, did they consider the totality? And they certainly considered all the data. It's not like they ignored the ABCDH (sic) Study. It's not like they said, "You know what? This data may not be great for us, so we are not even going to opine about it," or, "We're not going to tell you what the real results were." They gave you the results, they gave the analysis, they considered the weight and the totality of the evidence, and they also considered the VFX data, which is obviously data they felt was

supportive, and they also developed the modeling. I think, your Honor, that's all important to consider in the framework and the analysis of looking at it from the lens of either Lanigan in Massachusetts state court or under Millward here in the First Circuit.

JUDGE WOODLOCK: All right. I am going to shuffle off the stage.

THE CLERK: All rise.

(WHEREUPON, the Joint Daubert Hearing adjourned)

C E R T I F I C A T E

I, Brenda K. Hancock, RMR, CRR and Official Reporter of the United States District Court, do hereby certify that the foregoing transcript constitutes, to the best of my skill and ability, a true and accurate transcription of my stenotype notes taken in the matter of In Re: Fresenius GranuFlo Litigation, No. 1:13-md-02428-DPW.

Date: November 30, 2015

*/s/ Brenda K. Hancock*
Brenda K. Hancock, RMR, CRR
Official Court Reporter