- VOLUME 1 -

IN THE UNITED STATES DISTRICT COURT

IN AND FOR THE DISTRICT OF DELAWARE

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RECKITT BENCKISER PHARMACEUTICALS INC., RB PHARMACEUTICALS LIMITED, and MONSOL RX, LLC,	:	CIVIL ACTION
Plaintiffs,	:	
vs.	:	
TEVA PHARMACEUTICALS USA, INC.,	:	
Defendant.	:	NO. 14-1451 (RGA)

- - -

Wilmington, Delaware
Tuesday, November 3, 2015
8:30 o'clock, a.m.

- - -

BEFORE: HONORABLE RICHARD G. ANDREWS, U.S.D.C.J.

- - -

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Official Court Reporters

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PROCEEDINGS

(Proceedings commenced in the courtroom, beginning at 8:30 a.m.)

THE COURT: All right. Good morning, everyone. Please be seated.

I just wanted to say that I did look at the resumes' of all of the experts and I did read the amended statement of facts, which I took to be mostly resolving limitations so that there was no question that they're not in dispute. So with that, I'm ready to go.

Plaintiff, are you ready?

MS. BOURKE: Yes, your Honor. We are.

THE COURT: And defendants, you're ready?

MR. LOMBARDI: Yes, we are, your Honor.

THE COURT: All right. Let's have an opening statement.

MR. LADOW: Good morning, your Honor. Dan Ladow for the plaintiffs.

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Your Honor, opioid addiction is a major public health challenge, one that has grown to epidemic proportions with the increased use of painkillers, and this has led to a surge in addiction with a tripling of overdose deaths in recent years. And the plaintiff, Reckitt Benckiser Pharmaceuticals, which is now known as Indivior, but we'll be using Reckitt Benckiser Pharmaceuticals, or RBP through the proceedings, that's how all the documents are denominated, is the pioneer in opioid addiction treatment, and it has been a world leader in this treatment space for over 20 years.

Our co-plaintiff, MonoSol Rx, is the pioneer in the new area of pharmaceutical prescription films, and together, the two companies are addressing this crisis in addiction with the medication that's the subject of this case.

In 2002, the FDA approved RBP's opioid dependence treatment product, Suboxone tablets, which contain two active ingredients, buprenorphine and naloxone.

Buprenorphine is an opioid that

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can satisfy cravings and reduce opiate drug abuse and it's safer than other opioids, and naloxone is an opiate antagonist or opioid blocker that when taken orally does not produce an effect, but it's an abuse deterrent, so that if the patient abuses the drug and tries to inject it, it can put the patient into withdrawal.

Now, the tablets were a huge advance in treatment, but they had different disadvantages, the tablet dosage form, such as dissolution time, taste, subject to crumbling and being subject to abuse and diversion, such as by crushing them and trying to inject them or snort them or something like that.

Now, to provide patients with a significantly better dosage form and improved dosage forms, RBP's addiction medication experts joined forces with MonoSol's film technology experts to make Suboxone sublingual film, which is a new dosage form.

And you see here on the slide what this product look like. On the right-hand side, there's a picture of the eight-milligram film.

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And as you may recall from the Markman proceedings, it's placed in the mouth of the patient, it's mucoadhesive, it sticks under the tongue and then it dissolves rapidly in the mouth, and the buprenorphine active ingredient is absorbed through the oral mucosa.

Now, compared to tablets, Suboxone film dissolves faster, tastes better, does not crumble, and is less readily diverted and abused than tablets, and because of these advantages, it's preferred by both doctors and patients, and it's the leading medication for opioid dependence. And it's the very success of the film, your Honor, that has brought us here today, and it's why the defendants have copied it.

Now, prescription, prescription pharmaceutical films are a new dosage form. The major reason why they're so recent is that making them is very complex and they present challenges in formulation and manufacturing that are very different from tablets. And, in fact, no prescription pharmaceutical films were approved by FDA prior to just 2009. This is not

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like technology that has been around for decades. This is new stuff.

Now, defendants are going to point to things like Listerine strips and Chloraseptic strips that became available in the early to mid-2000s, but these are not prescription pharmaceutical films that need FDA approval and have to meet the uniformity standards that are associated with FDA approval.

And, in fact, sublingual film, the commercial product at issue here, was the very first sublingual film approved by the FDA in 2010, and this dosage form is so new, that these cases before this Court right now are the very first ANDA cases that involve a prescription pharmaceutical film.

Going to the patents, as your Honor knows, there are three Orange Book patents at issue in the case. Each of the three patents relates to a different aspect of pharmaceutical film innovation that resulted in Suboxone film, and the infringement and validity issues for each patent are really separate and distinct.

To just briefly introduce the

patents, the '514 patent solved the drug content uniformity problem in pharmaceutical prescription films. And as you can see here in this excerpt on the top, if you have a failure to achieve -- this is an excerpt from the patent -- a high degree of accuracy with respect to the amount of active in the cut film, this can be harmful to the patient. Of course, for safety reasons and efficacy reasons, you want the patient to get the right dosage.

And when the patent was filed, the inventors noted that about that world regulatory authorities required that the dosage amounts in dosage forms not vary by more than about ten percent of the desired amount of the active, and concluding that that basically mandates uniformity in the film. And what the present invention of the '514 provides, as it says in that last excerpt highlighted, is exceptionally uniform film products when attention is paid to reducing the aggregation of the compositional components.

I'm going to say a very brief, and really a very brief word about the '832 patent

since it at least relates in part to commercial success, which you'll be hearing about in this trial, but I'm not going to address it any further because infringement and validity of the '832 is going to be done in December.

THE COURT: All right.

MR. LADOW: This '832 patent is basically directed to the Suboxone film formulation, and the patent reports the inventor's surprising discovery about the absorption of buprenorphine, which was contrary to prior art teachings about pH partition theory, which you'll hear more about in December, and led directly to Suboxone film.

And as the first excerpt indicates, the point of the patent was to provide a new dosage form, a film dosage, that would be bioequivalent to Suboxone tablets, which had been on the market for some years.

The '150 patent, the '150 patent is relating to a polymer profile for fast dissolving, mucoadhesive pharmaceutical films, and it provides a pharmaceutical polymer profile for Suboxone film. And it teaches that if you

want to balance the properties of adhesion, the mucoadhesion in the mouth, dissolution, the good tear resistance, the strength of the film, that what you can do is include about 50 to 75 percent of low molecular weight polyethylene oxide, which you are going to hear a lot about, your Honor, or PEO, optionally combined with a small amount of a higher molecular weight PEO, with the remainder of the polymer component contains a cellulosic polymer like HPMC. So it provides this polymer profile that you need to do this.

Now, the '514 patent, the asserted claim are the ones that you see here, there's one independent claim, 62, and then four dependent claims, infringement of this patent, your Honor, is going to be addressed in December. We're just doing validity in this trial.

Plaintiffs' expert on the validity of the '514 patent is professor Robert Langer. He's an MIT Institute professor. He has over a thousand articles and issued patents and he's one of the most decorated scientists in our

country. He's an expert in the chemical engineering and pharmaceutical drug delivery forms.

The defendants' two main invalidity arguments are indefiniteness and obviousness. And before addressing indefiniteness, a little background first about the cast film process that relates to the pharmaceutical films that we're talking about. And basically that process, as Dr. Langer will explain, consists of about five basic steps. It's obviously a lot more complicated, but there are about five basic steps.

So the first one is that you dissolve one or more polymers into a solvent and then you mix it.

Step two, the active ingredient is mixed in, and you do that to form a, what's called a casting solution or a casting dispersion.

Step three, the casting solution is then cast by a roller, as you see here, onto a sheet in a continuous casting process, as depicted on the slide.

And then a conveyor belt moves the sheet through a controlled drying process, drying out the solvent, and this results in a dry film which is then cut into individual dosage units as you can see in the bottom illustration.

These are the claim terms we've highlighted that relate to the indefiniteness issue that defendants have raised with respect to this patent.

So as you can see on the top, it's a drug delivery composition. It's independent claim 62. Cast film comprising a flowable water soluble film forming matrix. And I'm going to skip down to the last clause, where the flowable film-forming matrix is capable of being dried without loss of substantial uniformity, and that the uniformity subsequent to drawing and casting of the matrix is this plus and minus ten percent of the desired amount that I mentioned before.

Now, Watson, defendants contend that the claims are indefinite because they say a final dried cast film cannot be flowable or

have a viscosity or be capable of being dried. But the final cast film is not required to be flowable, as the defendants assert.

As Dr. Langer will explain, the reference to flowable here in the claims can't mean that the final dried solid film is flowable. That wouldn't make sense to anybody let alone a person of ordinary skill in the art of this technology. Instead, what flowable clearly means is that the polymer matrix must be flowable during the casting process, as I showed on the other slide.

And the film is a cast film because it was made by a casting process. That's why it's called a cast film. And the final film, whose uniformity, as I said, must be within ten percent of the desired amount, is, as the claim says, subsequent to casting and drying of the matrix.

So the defendants' argument that the claim is indefinite because it supposedly requires the impossible that the final dried film also be flowable and that it also have viscosity and be capable of being dried even

though it has already been dried is contrary to the specification, it's contrary to common sense and how one of ordinary skill would understand this. What it really is, is a belated claim construction argument that we think should be rejected. And as Dr. Langer will testify, a person of ordinary skill in the art would have no trouble understanding the meaning of these claims in this context with reasonable certainty.

Turning to the defendants' obviousness argument, your Honor, a key challenge in film technology was the problem of achieving what we're going to refer to, and you're going to hear a lot about, drug content uniformity, or DCU, in a pharmaceutical film. In particular, prescription pharmaceutical film that has to be approved by the FDA.

Drug content uniformity must be maintained throughout the manufacturing process in order to meet FDA requirements and ensure proper dosing just as we talked about before so the patient gets the right amount of the drug, not too much, not too little. It has to be safe

and efficacious.

This was a major challenge because, as Professor Langer will explain, there are quite a few forces or gradients that can cause aggregation or migration of an active during the process, during those five steps that I described in making a cast film, including during mixing and including during casting and drying. And all of these different forces and gradients can cause aggregation that results in lack of uniformity of a film. And it was the '514 patent that was the first to solve this drug content uniformity problem in pharmaceutical films.

The '514 patent recognized, as Dr. Langer will explain to you, that by rapidly increasing viscosity and locking in the, locking in the active in place together with using controlled drying procedures to avoid aggregation, that you could produce the film having the requisite uniformity and drug content uniformity.

And as we see here in this excerpt, the patent is the '514 patent talks

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