

Recognizing this definition of “controlled release preparation,” however, does not end the inquiry as to whether the term in controversy constricts the type of dosing environment used to measure therapeutic effect. To decide that issue, the entirety of the claim must be examined in light of the specification. *Phillips*, 415 F.3d at 1315.

I conclude that the independent claims require that one tablet provide the claimed therapeutic effect. Defendants are correct that the general rule defining “a” to mean “one or more” does not apply here, so there is no basis for Plaintiffs’ presumption that the claims cover a repeated-dosing environment. Traditionally, “a” means “one or more” in “comprising” claims because “comprising” is an open transition phrase. *Scanner Techs. Corp. v. ICOS Vision Sys. Corp., N.V.*, 365 F.3d 1299, 1305-06 (Fed. Cir. 2004). “When a claim uses an ‘open’ transition phrase, its scope may cover devices that employ additional, unrecited elements.” *AFG Indus., Inc. v. Cardinal IG Co., Inc.*, 239 F.3d 1239, 1244 (Fed. Cir. 2001). The decision in *Baldwin Graphic Sys., Inc. v. Siebert, Inc.*, 512 F.3d 1338 (Fed. Cir. 2008), provides a good example of how the “one or more” rule should apply. The claim at issue read: “A pre-packaged, pre-soaked cleaning system ... comprising in combination: (1) a pre-soaked fabric roll ... said fabric roll having a sealed sleeve ... .” 512 F.3d at 1340. The Federal Circuit held that, absent anything in the record indicating a contrary meaning, “a pre-soaked fabric roll” was not limited to a single roll. *Id.* at 1343. Thus, the invention in *Baldwin Graphic*, a pre-packaged, pre-soaked cleaning system, could contain more than one pre-soaked fabric roll. Similarly, applying the rule

to the '887 patent might mean, for example, that a single tablet could contain something in addition to “a substrate” and “a controlled release coating” (including, for example, additional substrates or controlled release coatings). It does not mean, however, that additional tablets, the very invention that the claims define, can be used to achieve the required therapeutic effect.

Plaintiffs argue that because the phrase “said preparation” occurs after “comprising” the *Baldwin Graphic* rule nonetheless applies. But *Baldwin Graphic* itself warned, albeit in a scenario where the antecedent phrase could carry a plural meaning, that the use of a definite article (“said”) to refer to an antecedent phrase did not change the numerosity of the antecedent phrase. *Id.* at 1343. Thus, the use of the anaphoric phrase “said preparation” following “comprising” does not change the singular nature of the antecedent phrase “a controlled release oral pharmaceutical preparation.”<sup>19</sup>

Nothing else in the claims or the remaining intrinsic evidence leads me to a different conclusion. Plaintiffs’ reliance on the “suitable for dosing every 24 hours” language is not persuasive. This limitation is not in the '430 patent, and Plaintiffs acknowledged at oral argument that the differences in claim language between the

---

<sup>19</sup>Although a term in the preamble does not generally limit the claimed invention, that rule does not apply where, as here, the preamble provides an antecedent basis for “said preparation.” See *Rapoport v. Dement*, 254 F.3d 1053, 1059 (Fed. Cir. 2001) (“[W]ithout treating the phrase ‘treatment of sleep apneas’ as a claim limitation, the phrase ‘to a patient in need of such treatment’ would not have a proper antecedent basis.”).

patents, on this point at least, are irrelevant. (D.I. 249 at 20:14-15.) Because both parties agree that construction of this term should be the same for both patents-in-suit, I am unable to conclude that language missing from one of the patents dictates the dosing environment for both. But even if the language were in both patents, I agree with Defendants that a person of skill, reading the claim language at issue, would have no reason to link a drug's dosing regimen to the therapeutic effect provided by a single dose. (D.I. 162 at 9 ¶ 23.)

Indeed, the specification indicates that the dosing regimen provided in the claims relates not to a repetition of doses over several days to achieve a therapeutic effect but to the amount of tramadol released from one or two tablets during about 24 hours. The specification provides five tables that list different *in vitro* release rates in terms of the percentage of tramadol released over time.<sup>20</sup> ('887 patent at 1:41-2:50.) For each hour listed, each table provides a range of percentage of tramadol released. The release rates in Table 2 are suited for twice-a-day dosing and so are of less relevance to the meaning of "suitable for dosing every 24 hours." (*Id.* at 1:58-2:8.) However, the other four tables are either unaccompanied by a dosing regimen (Table 1) or suggest that the given release rates are suited for once-a-day dosing (Tables 3-5).

Table 1 reads as follows:

---

<sup>20</sup>Testing *in vitro* involves evaluating experimental formulations in fluids and under conditions that simulate to some extent the chemistry of the stomach and intestine. (D.I. 157 at 6.) Clinical testing in humans, in contrast, is called *in vivo* testing. (*Id.*)

TIME (H)	% RELEASED
1	0-50
2	0-75
4	3-95
8	10-100
12	20-100
16	30-100
24	50-100
36	>80

(*Id.* at 1:45-58.) According to this table, at hour 8, 10-100% of the tramadol from a single pill should be released.

Tables 3 and 4 list release rates that are “particularly suited for once-a-day dosings.” (*Id.* at 2:9-38.) The entries for hour 8 in those tables list 35-100% and 10-65% tramadol released, respectively.

Table 5, reproduced below, lists release rates that are “more preferabl[e]” for once-a-day dosing.

TIME (H)	% TRAMADOL RELEASED
1	15-25
2	25-35
4	30-45
8	40-60
12	55-70
16	60-75

(*Id.* at 2:39-50.) The amount of tramadol released at hour 8 in that embodiment is between 40-60%.

These tables indicate that the narrower the range of release, the more preferable the preparation is for once-a-day dosing. The same narrowing of range is present for all

the corresponding hours as the tables move from preparations that are less suitable for once-a-day dosing to preparations that are more suitable.<sup>21</sup>

Though not presented in the briefing by either side, it appears that the narrower release ranges in once-a-day preparations may reflect a safety concern. (D.I. 249 at 40:4-9.) More specifically, it appears that, unless the amount of tramadol released is predictably controlled, a large percentage of tramadol might be released from a first pill after a second pill is taken, that is, after 24 hours following ingestion of the first pill. If a second pill were to release a large amount at the same time, it might introduce an unsafe level of tramadol in the bloodstream. Arguably, this indicates a consciousness on the part of the patentee that multiple doses may be needed in some cases, perhaps because of continuing or chronic pain. But safety and efficacy, though related, are not one and the same. That the concentration of tramadol provided by one pill needs to be controlled in a multiple-dosing regimen does not mean that the overall amount of tramadol released from one pill cannot provide a therapeutic effect over a 24-hour period. And it is to that therapeutic effect that the claims speak.<sup>22</sup>

---

<sup>21</sup>Table 1 has the largest range of percentage tramadol released for each hour. Predictably, and entirely appropriately, claims 1 and 13 of the '887 patent claim this release rate, even though other tables list rates that are "suited for once-a-day dosing." By claiming a broad range of release rates, the claims still cover the narrower ranges found in the other tables.

<sup>22</sup>For the same reason, I decline to give the meaning Plaintiffs seek to the word "every" in the phrase "suitable for dosing every 24 hours." My understanding of "every 24 hours" is not that a tablet must be taken every 24 hours in order to achieve a

In sum, Plaintiffs' proposal would unduly broaden the patent claims. Nothing in the claims or the specification supports achieving the claimed therapeutic effect over the course of multiple doses. To the contrary, the claims list the elements of a single tablet, and every time the specification describes the results of administering controlled release tramadol to a human being it does so through the administration of a single tablet.<sup>23</sup>

Accordingly, I will construe the term "A [solid] controlled release oral [dosage form/pharmaceutical preparation/pharmaceutical tablet] ... said [dosage form/pharmaceutical preparation/coated tablet] providing a therapeutic effect for [at least] about 24 hours" to mean "a single tablet, not including additional or previously administered tablets, that provides a therapeutic effect for [at least] about 24 hours."<sup>24</sup>

---

therapeutic effect, but that tablets can effectively be used every 24 hours without safety concerns.

<sup>23</sup>Each side argues that its proposed construction is bolstered by an opinion in a separate patent infringement lawsuit brought by Purdue on an unrelated patent. See *Purdue Pharma L.P. v. Boehringer Ingelheim GmbH*, 98 F.Supp. 2d 362 (S.D.N.Y. 2000), *aff'd*, 237 F.3d 1359 (Fed. Cir. 2001). The claim at issue in *Boehringer* unambiguously stated that a certain pharmacokinetic parameter was to be measured "after repeated administration every 12 hours through steady-state conditions." 98 F.Supp. 2d at 369. The issue in *Boehringer* was whether a different claimed pharmacokinetic parameter was also to be measured in a repeated-dosing environment. *Id.* at 373. *Boehringer*, while being a thorough and thoughtful explanation of the issues before that court, does not help me resolve the present claim construction issue. To draw conclusions as to what lessons Purdue may have or should have gleaned from the prosecution of the patent in *Boehringer* or the subsequent litigation is too speculative an exercise. See *Medrad, Inc. v. MRI Devices Corp.*, 401 F.3d 1313, 1318 (Fed. Cir. 2005) (warning against basing construction on claim construction decisions from unrelated litigation).

<sup>24</sup>It is unnecessary to adopt Defendants' proposed construction to the extent it would include language guarding against measuring the therapeutic effect provided by

C. “therapeutic effect for about 24 hours after oral administration”

Having construed the term “therapeutic effect” I must still determine the meaning of the term “for about 24 hours after oral administration.” The parties’ dispute is over when the 24-hour period begins. This disagreement can be traced directly back to the parties’ dispute over the dosing environment within which therapeutic effect is to be measured. For the reasons just set forth, I have decided that therapeutic effect is to be measured with a single pill. That construction effectively eliminates the parties’ disagreement as to the meaning of “for about 24 hours after oral administration.”

Defendants, who argued that therapeutic effect should be measured in a single-pill environment, have proposed a construction in which the 24-hour period begins at the onset of action. (D.I. 161 at 1.) Plaintiffs’ counterargument that the 24-hour period is not linked to “when pain relief begins after the *first* dose” is predicated on measuring therapeutic effect in a repeated-dosing environment. (D.I. 157 at 21.) At the *Markman* hearing, however, Plaintiffs acknowledged that in a single-pill environment, therapeutic effect should be measured from when the treatment becomes effective. (D.I. 249 at 46-47.) Plaintiffs also recognize in their briefing that there is a lag between when a single pill is administered and when it takes effect. (D.I. 221, Exh. A at 7.) Because both sides

---

external sources such as a morphine drip. (D.I. 249 at 36:23-37:1.) Other than the numerosity of the tablet, Plaintiffs do not argue that something in addition to the tablet provides the required therapeutic effect, nor would that be a reasonable reading of the claims. As explained above, the claims themselves clearly dictate that it is the tablet alone that provides the contemplated therapeutic effect.

agree that the therapeutic effect provided by a single pill does not begin immediately, I will adopt a construction that starts the 24-hour period when the treatment begins to provide its intended effect.

At the *Markman* hearing, both parties opined that the phrase “after oral administration” does not add meaning to the term “therapeutic effect for about 24 hours after oral administration.” Plaintiffs acknowledged that they view the phrase as irrelevant (D.I. 249 at 19), and Defendants agreed, stating that the phrase does not add meaning (D.I. 249 at 34). While I am hesitant to accept that a claim term does not add meaning, in this case I believe the parties are correct. The phrase “after oral administration” simply communicates that the treatment is to be taken orally and will not take effect until after it has been administered. The patent specification states repeatedly that the invention is to be taken orally and it is obvious that the treatment will not take effect until it has been administered. For the reasons stated above, I will construe the term “for about 24 hours after oral administration” to mean “for about 24 hours from when the treatment begins to provide its intended effect.”

D. “therapeutic effect for at least about 24 hours”

This term is closely related to the term “therapeutic effect for about 24 hours after oral administration,” which I construed above. The terms are so similar that Defendants have proposed that they be defined exactly the same way. (D.I. 161 at 17.) Plaintiffs recognize the addition of the words “at least” and include them in their proposed

construction. (D.I. 157 at 22.) The words “at least” have a plain meaning and in this context indicate that the effect of the treatment could last longer than about 24 hours. Accordingly, and for clarity, I will construe the term “therapeutic effect for at least about 24 hours” to mean “an effective treatment for pain for about 24 hours, or longer, from when the treatment begins to provide its intended effect.”

E. “a pharmaceutically effective amount of tramadol or a salt thereof”

My construction of “therapeutic effect” largely resolves the parties’ disagreement over the “pharmaceutically effective” term. Defendants propose that this term means “[a]n amount of tramadol or its salt contained in the substrate or the normal release matrix to achieve a therapeutic effect.” (D.I. 247 at 4.) Plaintiffs object to Defendants’ proposal insofar as it seeks to import the placebo-controlled clinical evidence requirement from its proposal for “therapeutic effect.” (D.I. 249 at 86:3-20.) Since I have construed “therapeutic effect” so as not to require placebo-controlled clinical evidence – and I will not import that requirement into the “pharmaceutically effective” term for the same reasons<sup>25</sup> – Plaintiffs’ objection falls away.

Defendants provide no intrinsic or extrinsic support for their proposed requirement that the tramadol be “contained in the substrate or the normal release matrix.” Accordingly, I will construe “a pharmaceutically effective amount of tramadol or a salt

---

<sup>25</sup>Defendants acknowledge that “therapeutically effective,” “pharmaceutically effective,” and “analgesically effective” are synonyms. (D.I. 181 at 10 n.18.)

thereof” to mean “an amount of tramadol or its salt sufficient to achieve a therapeutic effect.”

F. “matrix”

1. The Parties’ Proposed Constructions

Plaintiffs propose that “matrix” means “A pharmaceutical preparation that incorporates the active ingredient dispersed within a solid dosage form.” (D.I. 247 at 8.) Noting that claim 1 of the ‘430 patent, the only asserted claim that uses the term “matrix,” uses the term only to refer back to the claim term “normal release matrix,” and that the specification describes both “normal release” and “controlled release” matrices, Plaintiffs contend that the term “matrix” must be broad enough to encompass either a “controlled release matrix” or a “normal release matrix.” Otherwise, Plaintiffs argue, the words “normal release” in the claim would be superfluous. (D.I. 157 at 15.)

Defendants maintain that the term “matrix” refers to a “system wherein a drug is incorporated into a polymer(s) structure by either particle or molecular dispersion, wherein the former is a suspension of drug particles homogenously distributed in the polymer(s) structure and in the latter drug molecules are dissolved in the polymer, and wherein drug release occurs by diffusion through and/or erosion of the polymer structure.” (D.I. 161 at 19.) Defendants contend that their proposed construction is in fact broad enough to encompass both types of release matrices. The dispute over this

term thus largely boils down to whether Defendants are correct that their proposal is sufficiently broad.

Urging that the intrinsic record is not informative as to the meaning of the term “matrix,” Defendants draw their construction from Yihong Qiu and Guohua Zhang, *Research and Development Aspects of Oral Controlled Release Technology*, 465, 466-67 (Donald L. Wise ed., 2000). Defendants argue that, as compared to Plaintiffs’ construction, their construction offers needed clarity on the concept of “dispersion.” (*Id.* at 20.)

Pointing to the testimony of their expert Dr. Martyn C. Davies, Plaintiffs contend that Defendants’ construction describes only “controlled release” matrices because it allows for drug release only through “diffusion” or “erosion.” (D.I. 157 at 16-17; D.I. 160 ¶ 34). Plaintiffs, like Defendants, resort mainly to the extrinsic record for their own construction, drawing their proposal from their expert’s opinion. (D.I. 157 at 15.) To the extent Plaintiffs rely on the intrinsic record, it is only to criticize the fact that Defendants’ construction limits the term “matrix” to polymer-based structures. Along these lines, Plaintiffs note that the specification describes controlled release matrices incorporating waxes and vegetable oils, which Plaintiffs contend are not necessarily polymers. (*See id.* at 15; D.I. 249 at 69-70; D.I. 160 ¶ 35.) Thus, Plaintiffs argue, even if one assumes that Defendants’ construction encompasses both “normal release” and “controlled release”

matrices, it is still wrong by virtue of its strictly limiting “controlled release” matrices to polymer-based structures.

## 2. The Court’s Construction

I agree with the parties that the term “matrix” must be construed broadly enough to encompass both a “controlled release matrix” and a “normal release matrix.” Turning first to Defendants’ proposed construction, the article by Qiu and Zhang from which Defendants draw their construction (D.I. 170, Exh. S), and, in particular, the precise section from which Defendants draw their construction, is describing only a “controlled release matrix.” Indeed, the article is entitled “Research and Development Aspects of Oral *Controlled-Release* Dosage Systems” and speaks on the topic of controlled release. (D.I. 170 Exh. S at 1 (emphasis added).) The precise section of the article from which Defendants ostensibly take their proposed construction is entitled “Common Oral Polymeric *Controlled-Release* Systems.” (D.I. 170, Exh. S at 5 (emphasis added).) Further, the introductory sentence of the specific paragraph from which Defendants take their construction even explains that “[b]oth hydrophilic and hydrophobic polymeric matrix systems are widely used to provide *controlled delivery* of drug substances ... .” (*Id.* (emphasis added).) In light of this, it seems plain that the Qiu and Zhang article, describing a system where drug release occurs by “diffusion and/or erosion,” pertains to controlled release. (*Id.*) Moreover, the Qiu and Zhang article was published roughly seven years after the effective filing date of the patents-in-suit. It is not authored by any

of the inventors, and, while I do not doubt that the authors are respected scientists, there is no apparent reason for taking the article to be especially authoritative in the field. In these circumstances, I am, to put it mildly, wary of relying on this extrinsic evidence to limit the scope of a disputed claim term.

Likewise, I am reluctant to adopt a construction that limits the term “matrix” to polymer-based structures. Defendants contend that I should adopt this aspect of their construction because the patent describes both “controlled release” and “normal release” matrices as being polymer-based. (D.I. 181 at 8-9.) With respect to the structures the patent describes as making up “controlled release” matrices (*see* ’887 patent at 3:48-67), Defendants contend that all of them would be understood by one of skill in the art to be polymers. (D.I. 181 at 9.) In support of that position, Defendants cite S. Venkatram et al., *An Overview of Controlled Release Systems*, 431, 443 (Donald L. Wise Ed. 2000), (D.I. 181 at 9 (citing D.I. 182, Ex. 1)), which, like the Qiu and Zhang article, was published roughly seven years after the effective filing date of the patents-in-suit, was not authored by any of the inventors, and does not appear unusually authoritative. I thus am not inclined to rely upon it to limit the scope of the claims.

Plaintiffs, pointing to the testimony of their expert, dispute the notion that the structures described in the patent as making up “controlled release” matrices are always polymers. For instance, Plaintiffs argue that “vegetable oils” are not always polymers. (*See* D.I. 157 at 15; D.I. 249 at 69-70; D.I. 160 ¶ 35.) The intrinsic evidence tends to

support Plaintiffs on this point. Specifically, in enumerating suitable materials for inclusion in a controlled release matrix, the patent lists “[h]ydrophilic or hydrophobic polymers” as a distinct and separate item from “vegetable oils and waxes.” (See '887 patent at 3:50-60.) Thus, even if some who are skilled in the art would understand that, in some contexts, “vegetable oils” are polymers, the patent indicates the possibility of non-polymeric vegetable oil based matrices. Accordingly, even if Defendants actually intended for their definition of “matrix” to cover only “controlled release” matrices, it would still be too narrow by virtue of it being limited to polymeric structures.

Furthermore, if I were satisfied that the patents-in-suit set forth only polymers as exemplary materials to incorporate in a “matrix,” I still would avoid limiting the scope of the claims based on nothing more than the absence of a more explicit reference to a non-polymeric matrix. See *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004) (requiring “explicit disclaimer” not just the “mere absence of any reference to [a] structure in the specification” to limit claim claim scope); *LG Philips LCD Co. v. Tatung Co.*, No. 04-343-JJF, 2007 U.S. Dist. LEXIS 43557, at \*24-\*25 (D. Del. June 15, 2007) (“The mere absence of a description of alternative embodiments in the common specification such as a flat screen monitor does not ... rise to the level of words of manifest exclusion or restriction.”) (citations omitted).

Finding no adequate reason to limit the term “matrix” to “polymeric” structures that provide drug release through “diffusion” or “erosion,” I conclude, as Plaintiffs

contend, that the term “matrix” means a “pharmaceutical preparation that incorporates the active ingredient dispersed within a solid dosage form.”

G. “normal release matrix”

Defendants contend that a “normal release matrix” is a matrix that “does not slow the release of the active ingredient.” (D.I. 161 at 20.) Plaintiffs offer a similar construction, contending that a “normal release matrix” “does not substantially slow the release of the active ingredient.” (D.I. 157 at 17 (emphasis removed).) Thus, the dispute over the meaning of the term appears to be a subtle disagreement as to the precise rate at which the matrix controls drug release. In any event, at the *Markman* hearing, both parties agreed that a “normal release matrix” releases the active ingredient as quickly as feasible. (See D.I. 249 at 83-84.) I shall thus construe the term “normal release matrix” to be “a matrix that releases the active ingredient as quickly as feasible.”

V. CONCLUSION

Accordingly, for the foregoing reasons, the disputed claim terms will be construed as follows:

<b>Claim Term</b>	<b>The Court’s Construction</b>
1. “therapeutic effect”	“an effective treatment for pain”

2. "A [solid] controlled release oral [dosage form/pharmaceutical preparation/pharmaceutical tablet] ... said [dosage form/pharmaceutical preparation/pharmaceutical tablet] providing a therapeutic effect for [at least] about 24 hours" "a single tablet, not including additional or previously administered tablets, that provides a therapeutic effect for [at least] about 24 hours"
3. "therapeutic effect for about 24 hours after oral administration" "an effective treatment of pain for about 24 hours from when the treatment begins to provide its intended effect"
4. "therapeutic effect for at least about 24 hours" "an effective treatment for pain for about 24 hours, or longer, from when the treatment begins to provide its intended effect"
5. "a pharmaceutically effective amount of tramadol or a salt thereof" "an amount of tramadol or its salt sufficient to achieve a therapeutic effect"
6. "matrix" "pharmaceutical preparation that incorporates the active ingredient dispersed within a solid dosage form"
7. "normal release matrix" "a matrix that releases the active ingredient as quickly as feasible"

November 4, 2008  
Wilmington, Delaware

IN THE UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF DELAWARE

PURDUE PHARMA PRODUCTS L.P., )  
NAPP PHARMACEUTICAL GROUP )  
LTD., BIOVAIL LABORATORIES )  
INTERNATIONAL, SRL, and ORTHO- )  
MCNEIL, INC., )

Plaintiffs/Counterclaim- )  
defendants, )

v. )

PAR PHARMACEUTICAL, INC., and )  
PAR PHARMACEUTICAL )  
COMPANIES, INC., )

Defendants/Counterclaim- )  
plaintiffs. )

Civil Action No. 07-255-KAJ  
(CONSOLIDATED)

**ORDER**

For the reasons set forth in the Memorandum Opinion issued today, IT IS  
HEREBY ORDERED that the following disputed claim terms of U.S. Patent Nos.  
6,254,887 (issued July 3, 2001) and 7,074,430 (issued July 11, 2006) are construed as  
follows:

**Claim Term**

“therapeutic effect”

**The Court’s Construction**

“an effective treatment for pain”

"A [solid] controlled release oral [dosage form/pharmaceutical preparation/pharmaceutical tablet] ... said [dosage form/pharmaceutical preparation/pharmaceutical tablet] providing a therapeutic effect for [at least] about 24 hours"

"therapeutic effect for about 24 hours after oral administration"

"therapeutic effect for at least about 24 hours"

"a pharmaceutically effective amount of tramadol or a salt thereof"

"matrix"

"normal release matrix"

"a single tablet, not including additional or previously administered tablets, that provides a therapeutic effect for [at least] about 24 hours"

"an effective treatment of pain for about 24 hours from when the treatment begins to provide its intended effect"

"an effective treatment for pain for about 24 hours, or longer, from when the treatment begins to provide its intended effect"

"an amount of tramadol or its salt sufficient to achieve a therapeutic effect"

"pharmaceutical preparation that incorporates the active ingredient dispersed within a solid dosage form"

"a matrix that releases the active ingredient as quickly as feasible"

  
CIRCUIT JUDGE

November 4, 2008  
Wilmington, Delaware