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**Datasheet for the decision  
of 27 July 2006**

**Case Number:** T 1103/03 - 3.3.02

**Application Number:** 95933919.3

**Publication Number:** 0781122

**IPC:** A61K 9/00

**Language of the proceedings:** EN

**Title of invention:**

Matrix for transdermal drug delivery

**Patentee:**

MINNESOTA MINING AND MANUFACTURING COMPANY

**Opponent:**

ADHESIVES RESEARCH, INC

**Headword:**

Matrix for transdermal drug delivery/MINNESOTA MINING

**Relevant legal provisions:**

EPC Art. 83

**Keyword:**

"Disclosure - sufficiency (no): Parameter defining decisive features of the subject-matter of the claim not measurable to compare with claimed values"

**Decisions cited:**

-

**Catchword:**

-



Case Number: T 1103/03 - 3.3.02

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.02  
of 27 July 2006

**Appellant:** MINNESOTA MINING AND MANUFACTURING COMPANY  
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**Representative:** Vossius & Partner  
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**Respondent:** ADHESIVES RESEARCH, INC  
(Opponent) Glen Rock  
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**Representative:** Burford, Anthony Frederick  
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**Decision under appeal:** Decision of the Opposition Division of the  
European Patent Office posted 28 July 2003  
revoking European patent No. 0781122 pursuant  
to Article 102(1) EPC.

**Composition of the Board:**

**Chairman:** U. Oswald  
**Members:** H. Kellner  
C. Rennie-Smith

## Summary of Facts and Submissions

I. European patent No. 0 781 122 according to European patent application No. 95 933 919.3, filed as WO 96/08229 based on the international patent application PCT/US95/12163, was granted with 10 claims.

Independent claims 1 and 9 as granted read as follows:

"1. A transdermal drug delivery device, comprising:

(1) a backing;

(2) a matrix adhered to one side of the backing and comprising

(a) a copolymer comprising

(i) one or more A monomers selected from the group consisting of alkyl acrylates containing 4 to 10 carbon atoms in the alkyl group and alkyl methacrylates containing 4 to 10 carbon atoms in the alkyl group; and  
(ii) optionally one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; and  
(iii) a macromonomer copolymerizable with the A and B monomers defined above and having a molecular weight in the range 500-500,000;

(b) a softener dissolved in the copolymer; and,

(c) if the softener is not therapeutically effective, a therapeutically effective amount of a drug,

wherein the structure and amount of the comonomers in the copolymer, the inherent viscosity of the copolymer, and the amount and structure of the drug and the softener are such as to provide the matrix with a

compliance value in the range  $2 \times 10^{-1} \text{ cm}^2/\text{N}$  ( $2 \times 10^{-6} \text{ cm}^2/\text{dyne}$ ) to  $4 \times 10^2 \text{ cm}^2/\text{N}$  ( $4 \times 10^{-3} \text{ cm}^2/\text{dyne}$ ).

9. A pressure sensitive skin adhesive comprising:

- (1) a copolymer comprising
  - (a) one or more A monomers selected from the group consisting of alkyl acrylates containing 4 to 10 carbon atoms in the alkyl group and alkyl methacrylates containing 4 to 10 carbon atoms in the alkyl group; and
  - (b) optionally one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; and
  - (c) a macromonomer copolymerizable with the A and B monomers defined above and having a molecular weight in the range 500-500,000; and
- (2) a softener dissolved in the copolymer,

wherein the structure and amount of the comonomers in the copolymer, the inherent viscosity of the copolymer, and the amount and structure of the softener are such as to provide the pressure sensitive skin adhesive with a compliance value in the range  $2 \times 10^{-1} \text{ cm}^2/\text{N}$  ( $2 \times 10^{-6} \text{ cm}^2/\text{dyne}$ ) to  $4 \times 10^2 \text{ cm}^2/\text{N}$  ( $4 \times 10^{-3} \text{ cm}^2/\text{dyne}$ )."

II. Opposition was filed against the granted patent under Article 100(a) and (b) EPC.

The following documents were cited *inter alia* during the proceedings before the opposition division and the board of appeal:

- (7) US 4 737 559

- (8) Ferry, J.D., "Viscoelastic properties of polymers"; second edition, New York: John Wiley & Sons, Inc., 1970, ch. 1, pages 4 to 15 and third edition, New York: John Wiley & Sons, Inc., 1980, ch. 6, pages 130 to 133 and 151
  
- (9) Van Holde K., Williams J.; "Study of the viscoelastic behavior and molecular weight distribution of polyisobutylene", Journal of polymer science, vol. XI, no. 3, pages 243 to 267
  
- (11) Report of Mr. Giles, University of Minnesota, dated 4 December 2003
  
- (13) Declaration of Scott Barnhart dated 21 July 2004
  
- (14) Satas D.; "Handbook of pressure sensitive adhesive technology", New York: Van Nostrand Reinhold, 1989, page 172, figure 8-14
  
- (15) Report of Mr. Giles, University of Minnesota, dated 9 March 2005

III. By its decision pronounced at oral proceedings on 25 June 2003 and posted on 28 July 2003, the opposition division revoked the patent under Article 102(1) EPC because neither the set of claims of the main request nor the sets of claims of the auxiliary requests I and II met the requirements of Article 83 EPC (sufficiency of disclosure).

The person skilled in the art desiring to put the invention into practice had to rely on the description of the test method to ensure measurement of the

compliance value J. In the present case, however, certain variables which undoubtedly had an influence on the measurement were not defined (clamping force between stationary plates; nature of backing material and of the sample plates; force applied on the folded "sandwiched" sample). The skilled person did not even know the temperature at which the test was performed. Having regard to the displacement X that had to be measured, small oscillations in temperature would certainly have an effect on the measurement.

- IV. The appellant (patentee) lodged an appeal against that decision. With its letter of 9 March 2006 it filed eight sets of claims as main request and auxiliary requests 1 to 7 replacing all previously filed requests.

The set of claims of the main request differs from the set of claims as granted only in that claim 9 is deleted and claim 10 consequentially amended. Independent claim 9 is also deleted in all of the following auxiliary requests.

In claim 1 of the set of claims of auxiliary request 1 the wording "which is a pressure sensitive skin adhesive" is added after "... (2) a matrix".

Claim 1 of the set of claims of auxiliary request 2 differs from claim 1 as granted in the wording

"; and wherein the drug is selected from the group consisting of antiinflammatory drugs, both steroidal and nonsteroidal, antibacterials, antiprotazoals, antifungals, coronary vasodilators, calcium channel blockers, bronchodilators, enzyme inhibitors, other

antihypertensives, leukotriene antagonists, anti-ulceratives, steroidal hormones, antivirals and/or immunomodulators, local anesthetics, cardiotonics, antitussives, antihistamines, narcotic analgesics, peptide hormones, cardioactive products, proteinaceous products, enzymes, anti-nauseants, anticonvulsants, immunosuppressives, psychotherapeutics, sedatives, anticoagulants, analgesics, antimigraine agents, antiarrhythmic agents, antiemetics, anticancer agents, neurologic agents, hemostatics, anti-obesity agents, as well as pharmaceutically acceptable salts and esters thereof"

added after " $(4 \times 10^{-3} \text{ cm}^2/\text{dyne})$ ".

In claim 1 of auxiliary request 3 both the amendments of auxiliary requests 1 and 2 are included.

In claim 1 of auxiliary request 4 a part of claim 8 as granted is introduced, defining a group of substances from which the softener is to be selected.

In claim 1 of auxiliary request 5 both the amendments of auxiliary requests 1 and 4 are included.

In claim 1 of auxiliary request 6 both the amendments of auxiliary requests 2 and 4 are included.

In claim 1 of auxiliary request 7 all the amendments of auxiliary requests 1, 2 and 4 are included.

For further details the original file should be consulted.

V. On 27 July 2006 oral proceedings took place before the board.

VI. As a main argument, the appellant submitted that the necessary parameters for the measurement of the compliance value were known from paragraph [40] in the patent as granted together with document (7) which was cited there.

With respect to the temperature at which the compliance value was to be measured, the appellant stated that this had to be done at ambient temperature, as was set out in document (7). Moreover the use temperature of the transdermal drug delivery device was room temperature and, with reference to the document (14), the compliance value of its matrix - around room temperature - would not vary, or vary only very minimally.

Finally, the appellant referred to the test report (11) and to the submitted data about comparative testing of compliance values (test report (15) together with the submissions in the letter dated 17 May 2005), the University of Minnesota and the patent proprietor having independently performed measurements on the same two kinds of samples.

The 8% difference in the average test results was well within the normal level of experimental variation and thus it was clear that the skilled person might readily perform compliance testing as described in the opposed patent with results that could be easily compared to the values enumerated in its claims.



VII. The respondents' arguments may be summarised as follows:

The decision of the opposition division was well founded, particularly with respect to parameters that were to be adapted because of the differences between the patent in suit and document (7) in the preparation of the samples (eg clamping force between stationary plates; nature of backing material and of the sample plates; force applied on the folded "sandwiched" sample).

Additionally, the respondent referred to document (9). The appellant had introduced this study itself to demonstrate that an apparatus for measuring compliance values was well known. In the view of the respondent, the description in document (9) of this apparatus provided detail of the kind missing from the opposed patent.

In particular, the "ambient temperature" referred to by the appellant could range from 18 to 25°C and in table V of (9) only 0.3°C difference in temperature caused significantly differing values in viscosities of polyisobutylenes. Therefore, the authors of (9) mathematically adjusted measured viscosity to a standard reference temperature of 35.0°C.

Summarising its arguments, the respondent stated that measured compliance values depended on the apparatus, on temperature and on pressure, but these parameters were not defined clearly and completely enough in the patent in suit to allow reproduction of the teaching of its claim 1. Of course the skilled person would be able

to measure some sort of compliance value for any matrix product produced with respect to this teaching, but this was useless as long it was not sure that for the same product sample the same result could be obtained as the appellant had obtained before filing its application.

VIII. The appellant requested that the decision under appeal be set aside and either that the patent be maintained on the basis of the set of claims filed as main request or, alternatively, on the basis of one of the sets of claims of the auxiliary requests I to VII filed with its letter of 9 March 2006, or that the case be remitted to the first instance for further prosecution.

IX. The respondent requested that the appeal be dismissed or, as auxiliary request, that the case be remitted to the first instance for further prosecution.

### **Reasons for the decision**

1. The appeal is admissible.
2. The amended claims filed by the appellant represent an attempt to overcome the objections raised by the respondent and the opposition division. Consequently, they are to be seen as a response to the arguments set out during the proceedings and are therefore admitted into the proceedings.
3. The features contained in the requested sets of claims may be derived from the application as filed (see originally filed claims 1 to 4, 6, 9, 13, 14, and 16 to

20 together with description page 3, lines 18 to 19, and page 12, line 7 to page 13, line 6) and from the patent as granted (see claims 1 to 10 together with description page 7, lines 20 to 41).

To that extent, the requested claims comply with the provisions of Article 123(2) and (3) EPC.

4. *Article 100(b) EPC*

4.1 *Main request*

4.1.1 Claim 1 of the main request is the same as claim 1 of the patent as granted.

4.1.2 It refers to a transdermal drug delivery device comprising a backing and a matrix.

The matrix is characterised by a range within which its "compliance value" is to be found.

- This matrix comprises a copolymer, a drug and/or a softener, these three compounds having been mixed in any way.
  
- The copolymer is not defined by its final chemical structure but by a definition of its constituents which are to be selected from at least two groups of substances, one of them being of monomeric nature (monomer A) and the other one being a polymer itself ("macromonomer"). To arrive at this copolymer, the constituents may be polymerised in any known and useful manner.

- Monomer A is to be selected from certain alkyl acrylates or alkyl methacrylates while the
- macromonomer is totally open in its chemical structure, the only characteristics being
  - a range for the molecular weight and
  - that it has to be copolymerisable with the other monomers.

Defining a claimed polymer product by its starting materials implying a well known polymerisation process is not in principle ruled out. In the present case, however, the so called compliance value of claim 1 represents a functional feature which is intended to characterise further

the chemical and physical structure and other physical properties

- of the starting material and
- of the final product of the polymerisation process, the copolymer, and
- of the matrix which is a mixture of this copolymer and the drug and/or softener.

This is directly confirmed by the wording of claim 1 that the "structure and amount of the comonomers in the copolymer, the inherent viscosity of the copolymer, and the amount and structure of the drug and the softener" **are such as** to provide the matrix with a compliance value in the range  $2 \times 10^{-1} \text{ cm}^2/\text{N}$  ( $2 \times 10^{-6} \text{ cm}^2/\text{dyne}$ ) to  $4 \times 10^2 \text{ cm}^2/\text{N}$  ( $4 \times 10^{-3} \text{ cm}^2/\text{dyne}$ )" (emphasis added by the board).

By this means, the parameter "compliance value" is considered to replace all further information, eg on the structure and amount of the comonomers in the copolymer, which would otherwise have been necessary to be able to obtain the claimed transdermal drug delivery device as a mixture of chemically well defined ingredients.

Consequently, in order to carry out an invention characterised by such a functional feature, the skilled person must be able to measure in a very clear and complete way the compliance value of any matrix he has produced according to all the features set out in claim 1 of the patent in suit with respect to this matrix (reproducible measurement on the same sample with the same apparatus under the same conditions) and he must be sure that the measured value is the same as the appellant had obtained for the same matrix before filing its application (repeatable measurement on another sample of the same kind with another apparatus, but under the same conditions).

- 4.1.3 To fulfil this requirement, in paragraph [40] on page 11 of the patent in suit the compliance value is defined by a mathematical equation and additional conditions are set out in respect of how the compliance values were measured.

The equation is

$$J = 2AX/hf,$$

"where A is the area of one face of the test sample, h is the thickness of the adhesive mass (ie, two times

the matrix thickness of the sample being tested), X is the displacement and f is the force due to the mass attached to the string".

Those conditions, however, are introduced together with the comment that "the compliance values given below were obtained by a modified version of the Creep Compliance Procedure described in U.S. Pat. No. 4 737 559 (Kellen)" (introduced into the proceedings as document (7)). The text following this introduction is characterised by a description of the modifications in the procedure of sample preparation, with no relation between the measuring parameters set out in (7) (see column 8, line 46 to column 9, line 34) and amendments made necessary by the modifications, and in particular with no indication of the temperature(s) at which the measurements were performed. Only by reference to (7) can the skilled person see that there the "J values" were measured at "ambient **conditions**", where inter alia the temperature for the measurement might or might not be meant (emphasis added by the board). The fact that the compliance values refer to a certain temperature is only mentioned in column 9, lines 6 to 7 of document (7): "The creep compliance at a given temperature is then calculated using the equation  $J_{(t)} = 2AX/hf \dots$ ".

- 4.1.4 Document (9) was referred to by the appellant as an example of the common general knowledge of the skilled person for measurements of compliance values.

There, in particular on pages 254 to 258, the compliance value is defined as

$\gamma/S$  (shear strain/shear stress)

(see page 254, under the heading "II. Viscoelastic behaviour of polyisobutylenes").

An apparatus corresponding in principle to the shear-creep rheometer to be used according to the patent in suit is described. This apparatus is used to obtain measurements of  $\rho'$  (corresponding to the displacement  $X$  in accordance with the formula  $X = \rho'f$ ) with respect to time. The corresponding compliance values  $J = \gamma/S$  can be obtained by conversion of  $\Delta'$  using equation (24), corresponding to the equation defining compliance values in the patent in suit (see (9), pages 255 to 257, chapters "Apparatus and experimental procedure" and "Calculations", in particular page 257, equation (24) and the following two lines, together with the submissions of the appellant in its grounds of appeal, page 10).

4.1.5 So far, definitions and working instructions with respect to the measurement of compliance values set out in (9) and in the patent in suit coincide. With respect to the influence of temperature on these measurements, however, in document (9) it is emphasised that

- curves of compliance values over time (equation (18) on page 254), obtained from constant stress experiments, will give a complete description of viscoelastic behaviour **at a given temperature**,
- both stress and **temperature** must be **maintained constant** throughout an experiment

and that therefore, the entire apparatus is placed in an air thermostat which maintains a temperature constant to within  $0.1^{\circ}\text{C}$  (see (9), page 255, lines 1 to 10 and page 256, lines 1 to 4).

These indications in (9) are in line with the well known fact that viscoelastic properties in general depend on temperature and they lead to the conclusion that compliance values have to be measured at exactly defined temperatures to be repeatable and reproducible.

Measurement under "ambient **conditions**", as far as it would really depend on a required temperature, would allow measuring in a wide range of temperatures. As far as "ambient **conditions**" would refer to the room temperature in a laboratory, a range of  $18^{\circ}\text{C}$  to more than  $25^{\circ}\text{C}$  is possible and as far as the temperature of the matrix while using the transdermal drug delivery device on the skin was concerned,  $35^{\circ}\text{C}$  would be appropriate. With this range of possible measuring temperatures being left open by the patent in suit, no reliable and comparable values for the compliance value can be obtained.

- 4.1.6 The main modification in the procedure of sample preparation in the patent in suit with respect to document (7) is that a "sandwich" configuration is built with matrix material between two layers of backing. For the measuring of the compliance value, consequently, the backing material is in contact with the plates of the apparatus and not the adhesive matrix material itself, as in the case of the measurements in document (7).



To apply the force to keep the matrix layers in place between the plates of the apparatus when stress is exerted on them by the weight, the teaching of document (7) sets a limit of approximately 10% of compression of these layers (see column 8, line 59 to 61).

Now, even if in the report (11) in the last but one sentence on the last but one page, it is "presumed" that "the 10% compression produces sufficient clamping force to hold the backing to a fixed position on the plates, so that it does not slip", in example 1 of (11) a 20% compression was performed (see (11), table on the last page). Even if the above mentioned equation  $J = 2AX/hf$  would have ruled out such an influence as long as a lower value of  $h$  is compensated by a higher value of  $f$  in a reciprocally proportional way, the teaching of (7) would imply that this was not the case when the compression exceeded "approximately 10%".

Therefore, in view of the teaching in document (7), even the compliance value measured in example 1 in report (11) is in doubt since it is not being measured by the rules set out in that document.

- 4.1.7 In the patent in suit, there is neither any exact definition of the measuring temperature with respect to the range for the compliance value set out in claim 1 nor any information on the measuring temperature of compliance values of the examples (see point 4.1.5 above).

Additionally, even with respect to the measuring parameters set out in (7) no information is given about

amendments made necessary by the modifications in the procedure of sample preparation (see point 4.1.6 above).

Under these circumstances, no reproducible and no repeatable results can be obtained for measurements of the compliance values featuring in claim 1.

4.1.8 In the circumstances of the case, the arguments of the appellant cannot succeed:

- (a) Citing document (14), the appellant wanted to submit that the use temperature of the transdermal drug delivery device of the patent was room temperature, and accordingly, its modulus and inversely the compliance value of its matrix - around this room temperature - would not vary, or vary only very minimally.

This submission could allegedly be derived from figure 8-14 on page 172 of this citation and - implicitly by reference to "a plateau in modulus" - from figure 8-13 and the description of figure 8-13 where "plateau modulus values" for a strapping tape adhesive and a freezer tape adhesive are mentioned (see (14), page 172 and bottom of page 171).

The description for figure 8-14 says that the requirement for a good pressure sensitive adhesive was "a 1-sec creep compliance greater than  $1 \times 10^{-6} \text{ cm}^2/\text{dyne}$  (Fig. 8-14)". Notwithstanding the observations that figure 8-14 - has no value indicated on the temperature scale,

- indicates a value of " $\log D(1) \cdot \text{Pa}^{-1}$ " on the other scale which at least does not rule out that the 1-sec creep compliance could be meant, and
- does not say what the two graphs in the figure refer to (one of them showing a "plateau" much less than the other)

the fact that the whole statement refers to a 1-sec creep compliance and not to a 3-minute compliance value as in the patent in suit is enough to make all conclusions so doubtful as to be worthless.

Figure 8-13, showing the graphs of modulus values for the two mentioned tapes, was referred to by the appellant not explicitly, but implicitly by the nature of its arguments. As far as these graphs did in fact show a plateau for the modulus on the logarithmic (*sic*) scale (at least for the strapping tape), no conclusions about 3-minute compliance values of pressure sensitive adhesives of transdermal drug delivery devices could be drawn because even the appellant's submission that the modulus was the inverse of the compliance value is only true for perfectly elastic solids and not for viscoelastic materials (see (8), page 11, paragraph under equation (12)).

- (b) The comparative testing (see test report (15) together with the submissions in the appellant's letter dated 17 May 2005) was intended to show that, solely on the basis of parameters for compliance value testing as described in the patent in suit, two different laboratories achieved the same results for the same kind of sample.

The results of the University of Minnesota were described in the report (15) with a reference to report (11) for further details with respect to the apparatus (see (15), page 1, first paragraph after "Reference", lines 2 and 3 together with paragraph 2).

The results of the appellant were reported by its representative in the letter of 17 May 2005.

While report (15) is silent about the temperature of the measuring, in the representative's report there are no precise details about the percentage of compression of the samples for clamping: "The test samples were lightly clamped between two stationary plates ..." (see letter of 17 May 2005, page 8, paragraph 2.2.2, lines 4 to 5).

Thus, the results of the comparative testing in fact cannot be compared and it is not necessary to discuss whether 8% difference in the average test results as reported was within the normal level of experimental variation or not.

#### 4.2 *Auxiliary request 1*

Since claim 1 of the set of claims of auxiliary request 1 differs from claim 1 of the main request only in the wording "which is a pressure sensitive skin adhesive" which is added after "... (2) a matrix" the reasons and conclusions set out for the main request apply equally.

Even if the words "pressure", "sensitive" and "adhesive" from the description for figure 8-14 ("the requirement for a good pressure sensitive adhesive") now appear in the claim, the conclusions drawn by the appellant are not valid because of the reasons set out under point 4.1.8(a) of this decision.

4.3 *Auxiliary requests 2 to 7*

The feature that the matrix of the claimed transdermal drug delivery device should be provided with a compliance value in a defined range is present in claims 1 of all these requests with identical meaning.

Therefore, all the arguments set out in this decision with respect to the main request and to the first auxiliary request apply equally to these requests as well.

5. Accordingly, the invention as claimed with respect to all requests of the appellant is not disclosed in the patent as granted in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (Article 100(b) EPC).

**Order**

**For these reasons it is decided that:**

The appeal is dismissed.

The Registrar:

The Chairman:

A. Townend

U. Oswald