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Unser Zeichen Our Ref.

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Bitte in der Antwort angeben
Please quote in your reply

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18 December 2008

Re: Opposition to the European Patent EP 1 429 795
(European Patent Application 02 777 223.5)
by Dr. Willmar Schwabe GmbH & Co. KG

The notice of opposition (Rule 79(1) EPC) dated 13 June 2008 refers:

I.

1. Introduction

Notices of opposition have been filed against the European Patent EP 1 429 795 B1 of the Dr. Willmar Schwabe GmbH & Co. KG company (hereinafter the patent in-suit) by Frutarom Schweiz AG (opponent 01), the African Centre for Bio-safety et al. (opponent 02), Alpinamed AG (opponent 03) and Finzelberg GmbH & Co. KG (opponent 04).

Opponent 01 files objections under Articles 54, 56 and 83 EPC. Opponent 02 files objections under Articles 53(a), 53(b), 54, 56 and Article 83/84 EPC. Opponent 03 files objections under Articles 54 and 56 EPC. Opponent 04 files objections under Articles 54 and 56 EPC.

2. The cited prior art

In order to ensure uniform designation of the cited documents in the following opposition procedure, the proprietor of the patent proposes the following numbering scheme for the documents:

		O I	**O II**	**O III**	**O IV**
D1	The Medical Plant Industry (R.O.B. Wijesekera, ed.) (1991), CRC Press, Inc. USA; Page 210	D1			
D2	Williamson E.M., DT. Okpako and F.J. Evans, (1996) Pharmacological Methods in Phytotherapy Research Vol. I., Selection, Preparation, and Pharmacological Evaluation of Plant Material, John Wiley & Sons Ltd. UK; Chapter 3, "Preparation of Plant Material", Pages 15 to 23	D2			
D3	Kolodziej H. and 0. Kayser (1998) “Pelargonium sidoides DC”, Zeitschrift für Phytotherapie, 19, Pages 141 to 151	D3			D1
D4	Kolodziej H., 0. Kayser and M. Gutmann (1995) “Arzneilich verwendete Pelargonien aus Südafrika”, Deutsche Apotheker Zeitung, 135, Pages 853 to 864	D4			
D5	Bladt S. (1977) “Umckaloabo - Droge der afrikanischen Volksmedizin”, Deutsche Apotheker Zeitung, 117, Pages 1655 to 1660	D5			
D6	By Bojanowski W. (1937) “Das Biologische Tuberkulosemittel Umckaloabo”, Fortschritte der Medizin, 55, Pages 141 to 145	D6			
D7	EP 0 692 257 A1	D7			
D8	*Adrien Sechehaye,* The treatment of pulmonary and surgical tuberculosis with Umckaloabo, B. Fraser & Co., London 1930, Pages 37 to 41		1)		
D9	*Bladt S., Hildebert Wagner, (1988),* “Cumarindrogen, 1. Mitteilung: Qualitätsprüfung der Umcka-Droge und ihrer Zubereitungen”, Deutsche Apotheker-Zeitung, 128, Pages 292-296		2)		

D10	Hagers Handbuch der pharmazeutischen Praxis, Vol. 2 Methoden, 5th edition, Berlin 1991, Pages 407-409		3)		
D11	European Pharmacopoeia, Third Edition, Strasbourg, June 1996, Page 837		4)		
D12	European Pharmacopoeia, Fourth Edition, Strasbourg, 20 September 2001, Pages 508/509		5)		
D13	Affidavit Dr. Stafford		6)		
D14	Affidavit Milile Rwexu		7)		
D15	Homöopathisches Arzneimittelverzeichnis, Edition 9, 1992, Page 51, Column 1 and 3			D1	
D16	Homöopathisches Arzneibuch, Vorschrift 4a, 3rd Supplement (H)13, 1985 and 5th Supplement (H)9, 1991			D2	
D17	Deutsches Arzneibuch 10, 1st Supplement 1992, Tinkturen und Extrakte			D3	D8
D18	Pharmacopoe Helvetica VII, 1996, Page 173, Page 221			D4	
D19	Analytik biogener Arzneistoffe, 2000, Wissenschaftl. Verlagsgesellschaft mbH Stuttgart, Section 1.1 - 1.24			D5	
D20	Fundamentals of Analytical Chemistry, 1976, Pages 631-635			D6	
D21	Schüler Duden Chemie, Dudenverlag, 1995, Page 140			D7	
D22	Das Neue Lexikon in 10 Bänden, Weltbildverlag, 1987, Pages 3798-3799			D8	
D23	Kayser O., Kolodziej, H., “Antibacterial Activity of Extracts and Constituents of Pelargonium sidoides and Pelargonium reniforme”, Planta Medica 63, 1997, Pages 508-510			D9	
D24	Haidvogl, Schuster R. and Heger M., “Akute Bronchitis im Kindesalter”, Zeitschrift für Phytotherapie, 17, 1996, Pages 300-313			D10	D2

D25	Umckaloabo Stevenskur, excerpts from the Red List				D3
D25a	Red List 1980				D3a
D25b	Red List 1983				D3b
D25c	Red List 1988				D3c
D25d	Red List 1992				D3d
D26	Lehrbuch Gaedcke / Steinhoff, Phytopharmaka, Wissenschaftliche Verlagsgesellschaft mbH Stuttgart, 2000, Pages 48-59				D4
D27	Lehrbuch Rudolf Voigt, Pharmazeutische Technologie -Für Studium und Beruf, Deutscher Apotheker Verlag Stuttgart, 2000, Pages 444-449, 452-455				D5
D28	Hagers Handbuch (E. Nürnberg / P. Surmann), Methoden, Springer Verlag, 1991, Pages 403-411				D6
D29	Hagers Handbuch der Pharmazeutischen Praxis, 1925, Julius Springer publishers, 1925; “Extrakta”, Eigenschaften von Extrakten und Verfahren zu ihrer Herstellung, Pages 1219-1230				D7
D30	Lehrbuch H. Kaiser, W. Lang, H. Spegg “Der pharmazeutisch-technische Assistent”, Deutscher Apotheker-Verlag, Stuttgart, 1970, Pages 309-313				D9
D31	Hunnis Pharmazeutisches Wörterbuch, Walter de Gruyter, 8th Edition, 1998, Page 1176				D10
D32	Tade Matthias Spranger, “Indigene Völker, 'Biopiraterie' und Internationales Patentrecht”, GRUR 2001, Pages 89-92				
D33	T. Brendler, B.-E. Van Wyk, “A historical, scientific and commercial perspective on the medicinal use of *Pelargonium sidoides* (Geraniaceae)”, J. Ethnopharmacol., 119 (2008) 420-433				

Documents D3 and D24 cited in the opposition procedure are documents D1 and D2 explicitly recognised in the examination procedure. Documents D32 and D33 are introduced in the opposition procedure by the proprietor of the patent.

3. Requests

The proprietor of the patent presents Claims 1 to 5 in accordance with the main request, on which the further opposition procedure is to be based.

The proprietor of the patent requests that the European Patent EP 1 429 795 be maintained in the entirety of the main request and that the notices of opposition be rejected.

An alternative oral hearing is furthermore requested in case the opposition division should intend to revoke the European Patent EP 1 429 795.

Main request:

Claim 1 of the main request reads:

"1. Process for the manufacture of a Pelargonium sidoides and/or Pelargonium reniforme extract,
characterised by
the Pelargonium sidoides and/or reniforme roots either
a) being subjected to percolation with an aqueous ethanolic solvent,
the drug residue optionally being slightly squeezed
and the raw extract optionally filtered,
whereby the substance is mashed with an aqueous ethanolic solvent before the actual percolation,
and the mashing and percolation is performed with different concentrations of aqueous ethanol, whereby the weighted average concentration of the aqueous ethanol used in the mashing and percolation is in the range of 10-92 % by weight, or

b) being subjected to a two-step maceration with an aqueous ethanolic solvent,
wherein the extract solution is filtered after the first maceration and the drug residue is macerated a second time and the extract solutions are combined after a solid/liquid separation,
wherein the aqueous ethanolic solvent is 10-92 % ethanol by weight."

Claim 1 of the main request is therefore based on a combination of the granted Patent Claims 1, 3, 4, 5 and 7.

Claim 2 of the main request is based on the granted Claim 2, Claims 3 and 4 of the main request are based on the granted Claims 6 and 7 and Claim 5 of the main request is based on the granted Claim 8.

4. The patent in-suit

The patent in-suit relates to a process for the production of extracts from the roots of *Pelargonium sidoides* and/or *Pelargonium reniforme*.

Pelargonium sidoides is a plant that has traditionally been used in southern Africa for a long time, as medication for gastrointestinal complaints and respiratory diseases, including tuberculosis; refer Paragraph [0002] of the patent in-suit.

The main ingredients of *Pelargonium sidoides* roots are Proanthocyanidines, comprising catechin and gallocatechin components. Simple cumarins are furthermore present, with a generally high degree of oxygenation of the cumarin base structure. This appears to be a structural characteristic typical of Pelargonium, see Paragraph [0005] of the patent in-suit.

In prior art, extracts from the *Pelargonium sidoides* and/or *reniforme* roots were generally produced for instance by simple maceration using acetone/water 4/1 (Kayser, O., Kolodziej, H., Phytochemistry 39, 1181-1185 (1995)) or pure methanol using the Soxhlet method (D9).

Pure aqueous extracts were also used (D3) for therapeutic purposes. An ethanolic extract of *Pelargonium reniforme*/*sidoides,* diluted with glycerine, is available in the trade (Red List 2001); refer Paragraph [0006] of the patent in-suit.

The process under Claim 1 of the main request, however, refers to a very special process for the production of an *Pelargonium sidoides* and/or *Pelargonium reniforme* extract, characterised by the *Pelargonium sidoides* and/or *reniforme* roots being either a) subjected to percolation using an aqueous ethanolic solvent and the drug residue being optionally slightly squeezed and the raw extract being optionally filtered, wherein the substance is mashed with an aqueous ethanolic solvent before the actual percolation and the mashing and percolation is carried out with different concentrations of aqueous ethanol, wherein the weighted average concentration of the aqueous ethanol used for the mashing and percolation is in the range of 10-92 % by weight, or b) a two-step maceration using an aqueous ethanolic solvent wherein the extract solution is filtered off and the drug residue is macerated a second time and the extract solutions are combined after the solid/liquid separation and the aqueous ethanolic solvent is 10-92 % ethanol by weight.

This is a special extraction procedure not disclosed in any of the cited documents and not obvious from the cited documents of prior art, refer Sections III. and IV. below.

In accordance with Paragraph [0007] of the patent in-suit, the extraction methods up to now have disadvantages of relatively low yields or serious temperature dependence (Soxhlet). In accordance with the explanations in Paragraph [0008] of the patent in-suit, it is the purpose of this invention to provide an improved gentle process for the production of *Pelargonium sidoides* and *Pelargonium reniforme* extracts, with a higher yield of extracts and simultaneously improving the effect of the extracts.

In accordance with the further explanations in Paragraph [0009] of the patent in-suit (lines 50-52), the extracts obtained in accordance with the invention have a total phenol content of at least 15%, preferably at least 18% after drying. Such extracts are particularly well suited for the treatment of acute and chronic inflammatory diseases and infections.

The results of examples 1 to 4 of the patent in-suit, in which a percolation was performed with different extraction solvents, show unexpected surprising effects for the process claimed in accordance with the invention.

The extract pursuant to example 1 in accordance with which initial mashing with 35 % ethanol by weight was performed before percolation with 5 % ethanol by weight yielded:

- an excellent yield of 18.4 % (the highest yield of all the examples and comparative examples named in the patent in-suite document);
- a high total phenol content of 17.47 % in the extract, and therefore well suited for the treatment of acute and chronic inflammatory diseases and infections, with the highest total cumarin content (3.18 %) of all the measured values in the examples and comparative examples given in the patent in-suit, whereby the total cumarin contents overall do not differ much, irrespective of the process and solvent used;
- a very good antioxidative potential, higher than that found for the comparative extracts and also higher than the antioxidative potential found for an extract obtained by two-step maceration with a solvent of comparable concentration (11 % EtOH by weight);
- in addition, an IC_{50} value for elastase inhibition far below that found in the comparative examples and also below that found in example 5 (two-step maceration with 11 % ethanol by weight); finally, the IC_{50} value of 5.7 for elastase inhibition is also the lowest value found in the percolation examples.

The results of examples 5 to 9 of the patent in-suit, in which maceration was performed in accordance with the invention with different extraction solvents, furthermore also show unexpected surprising effects for the process claimed in accordance with the invention.

Compared to the results following maceration pursuant to DAB *[German Pharmacopoeia]* (comparative example 1), these examples show:

- a clearly higher yield,
- a clearly higher total phenol content,
- a comparable practically constant total cumarin content,
- a pronounced and clearly improved antioxidative potential as well as
- a clearly reduced IC_{50} value for the elastase inhibition.

The results of examples 1 to 4 and 5 to 9 of the patent in-suit therefore unequivocally prove that the target of providing an improved process to extract higher yields with simultaneously improved effect of the extracts has been achieved.

II. Exceptions to patentability (Articles 53 a) and b) EPC)

Opponent 02 uses this opposition procedure to refer to the Convention on Biological Diversity (CBD) and accuses the proprietor of the patent of “Biopiracy” (although he avoids the use of this term).

As far as can be ascertained, he refers to EPC Articles 53(a) and (b) as the legal basis under the EPC.

1. Introduction to the Convention on Biological Diversity (CBD)

The Convention on Biological Diversity is an international agreement on the environment negotiated at a United Nations Conference on the Environment and Development in Rio de Janeiro in 1992.

The CBD has three equally important objectives:

- protection of the biological diversity,
- sustainable utilisation of its components,
- regulation of access and fair compensation for advantages arising from the use of genetic resources.

As repeatedly and specifically highlighted in various provisions, the Convention contains only framework provisions and requires implementation by national legal regulations. To date, these framework regulations have not, however, been implemented in law.

There is also no direct interrelation between the access and participation arrangements of the Convention on Biological Diversity and the effectiveness of patents. In the European Union, only recital 27 of the Biotechnological Directive 98/44/EC, dated 6 July 1998, on the legal protection of biotechnological inventions needs to be referred to in this respect. It is stated there:

> *"Whereas if an invention is based on biological material of plant or animal origin or if it uses such material, the patent application should, where appropriate, include information on the geographical origin of such material, if known; whereas this is without prejudice to the processing of patent applications or the validity of rights arising from granted patents."*

An overview over the relationship between the CBD provisions and patent law is given in the article by Tade Matthias Spranger, “Indigene Völker, 'Biopiraterie' und Internationales Patentrecht”, GRUR 2001, Pages 89-92 (presented as document **D32**). Paragraphs that are important for the understanding of this relationship are reproduced in part below.

> *“The provision under Article 16 III of the Convention is of cardinal importance to the implications under patent law. In accordance with this provision, each contracting party shall, where appropriate, take regulatory, administrative or political measures to grant contracting parties that make genetic resources available access to technology or to allow them to pass on such technology utilising said resources, at mutually agreed conditions. This accessibility option is intended to be available especially with respect to developing countries and also includes technology protected through patents and other intellectual property rights. It is self-evident that this provision significantly impacts on intellectual property rights. Article 16 V of the Convention for this reason states:*
>
> *“The contracting parties, recognising that patents and other intellectual property rights may have an influence on the implementation of this Convention, shall cooperate in this regard subject to national legislation and international law in order to ensure that such rights are supportive of and do not run counter to its objectives.”*
>
> *The confusion is now perfect. On the one hand, “accessibility” also to patented technologies is to be virtually enforced and, on the other hand, a harmony is to be established between the Convention and intellectual property rights.*
>
> *The base standard of the World Trade Organisation TRIPS agreement (Agreement on Trade-Related Aspects of Intellectual Property Rights) is, however, already in conflict with this approach, since it states that patent protection must be guaranteed for products and processes in all fields of technology.*

Article 2711 TRIPS provides that, subject to Par. 2 and 3, it shall be ensured that patents can be granted for inventions in all fields of technology. This is applicable both to products and to processes, provided that they are new, involve an inventive step and are susceptible of industrial application. Article 2712 adds that patent rights shall be available and enforceable without discrimination with respect to the place of the invention, the technical field or whether the products are imported or produced locally. Limited patent protection for inventions based on genetic resources of a certain origin is therefore hardly feasible."

[…]

"Overall, it must therefore be recognised that Article 16 of the Convention on Biological Diversity, despite ambiguous wording, protects intellectual property rights. […] The European Union, being a contracting party to the Convention on Biological Diversity, also explicitly pointed out that the rights to access and transfer pursuant to Article 16 of the Convention are subject to adherence to the principles and rules governing intellectual property. The accusation that this interpretation violates the fundamental principles of the stipulations under Article 16 III may be countered by the argument that the general demand to facilitate access to technology remains. To achieve this target it is, however, not necessary to amend international patent law."

[…]

"So-called "Biopiracy" is not a problem of patent law, but is probably a direct result of actual conditions in many so-called third world countries. Most of the affected countries did not effectively prevent access to their genetic resources in the past, but they now react by lamenting the exploitation of their genetic diversity and then continue by demanding participation in the economic advantages.

This attitude is the equivalent of "venire contra factum proprium". A practical solution must therefore be found on another level. In this respect, the focus should shift from international regulatory mechanisms. The problem can and must be resolved on a national level. The following is often ignored in ongoing discussions: Every individual country has a right to prohibit third parties from exploiting its genetic resources. This – national – route represents the only possibility of counteracting undesirable excesses in the use of genetic resources by industry (countries) without detrimental system breakdown. Filing for a patent is certainly costly and highly formalised. It is obvious that the indigenous peoples cannot even begin to meet the existing requirements. This circumstance cannot, however, be used to burden the proven patenting system, which to a significant degree relies on the idea of legal security, with a considerable uncertainty factor by adapting the conditions to the requirements of local communities."

2. Response to the accusation of Biopiracy

Lacking corresponding legal bases under the CBD, Opponent 02 accuses the proprietor of the patent of "Biopiracy", based on EPC Articles 53(a) and (b) (although he avoids using the term in his written submission of opposition).

This accusation by Opponent 02, supposedly based on the CBD, is both legally and morally untenable and arbitrary, stating falsehoods with respect to patent law and other facts.

2.1 The proprietor of the patent, although not legally obliged, complies with the CBD stipulations, also meeting the optional requirements to state the geographical place of origin of the material used in accordance with the invention; refer recital 27 of the Biotechnological Directives, as implemented in § 34a of the German Patent Law.

§ 34a PatG *[German Patent Law]* reads as follows:

> *"If an invention is based on biological material of plant or animal origin or if it uses such material, the patent application should include information on the geographical origin of such material, if known. This is without prejudice to the processing of patent applications or the validity of rights arising from granted patents."*

This provision is firstly only a directive and secondly it is clearly stated there that non-compliance with this directive does not affect the processing of the patent application or the validity of the rights under the patents granted.

Since there is no corresponding arrangement in the EPC, European patents are therefore under no legal obligation in this respect, not even in the form of a directive.

The proprietor of the patent, on the other hand, voluntarily meets the stipulation of stating the geographical place of origin in his patent applications and patents and refers, for instance, in this patent in-suit on Page 1, Paragraph 2, to the fact that *Pelargonium sidoides* is a plant traditionally used as a medicine in southern Africa to treat gastrointestinal complaints and respiratory diseases, including tuberculosis. The term "southern Africa" was used because *Pelargonium sidoides* is endemic not only to South Africa but also to Lesotho. Later publications, on the other hand, show that bronchitis and colds are not part of traditional knowledge (T. Brendler, B.-E. Van Wyk, J. Ethnopharmacol., 119 (2008) 420-433 (**D33**)).

In this patent, the proprietor of the patent therefore also complies with the "compulsory regulation" of Article 49a of the Swiss Patent Law, to which Opponent 02 referred in Section 1 on Page 2 of his written submission of opposition. It should in this respect also be noted that this Article only came into force on the 1st of July 2008, almost six years after the date of filing, i.e. seven years after the priority date of the patent in-suit came into force.

The proprietor of the patent therefore complied with the requirement to name the geographical origin years before this requirement was made compulsory under Swiss law - an attack against the proprietor of the patent on these grounds therefore appears quite absurd.

The fact that South Africa had no provision regulating access to the use of biological resources before 1 April 2008 is further evidence of the absolute lack of justification for the demands of Opponent 02 in this respect. Benefit Sharing Agreements and Material Transfer Agreements are components of this regulation as well.

The proprietor of the patent filed the requisite application with the responsible government department within the legally prescribed period.

The assertion of Opponent 02 that the CBD provisions were enacted in South African law at the time the patent was filed in September 2002 already, is therefore also disproven; refer to misleading statements by Opponent 02 on Page 1, last paragraph of the written submission of opposition.

2.2 To summarise: firstly, the provisions of the CBD are not a legally obligatory framework under the European Patent Convention and secondly, the proprietor of the patent has voluntarily and as a matter of course complied with the requirement to name the geographical origin in filing his patent and has, as soon as possible after the corresponding regulation came into force in South Africa ($5^1/2$ years after filing the patent in-suit), made the necessary application without delay.

It should furthermore be specifically pointed out that the collection and export of *Pelargonium sidoides* from South Africa and Lesotho obviously has the explicit approval of the relevant authorities. The proprietor of the patent is in possession of the relevant collection and export permits.

2.3 It is also a principle of the proprietor of the patent not to exploit traditional knowledge or use with any of his patents, irrespective whether these were passed down in writing or verbally.

It is in no way the intention of the proprietor of the patent to prevent the traditional use of a biological, biochemical or genetic resource with his patents, or even to protect the resource itself.

The research activities of the proprietor of the patent greatly benefit the donor country, since they are a prerequisite for the approval of medicines and therefore for marketing in most countries.

The company operates globally, cultivating also in South Africa, and as such the proprietor of the patent has instituted several “Benefit Sharing” measures that are sensible and necessary in the view of the company.

The activities are centred around:

- sustainable and responsible collection of *Pelargonium sidoides* based on valid collection permits to ensure the long term survival of the plant in its habitat,

- creating a sustainable and significant income for the communities collecting *Pelargonium sidoides*,

- creating know-how and sustainable income in South Africa through controlled cultivation and

- research projects with partners in South Africa.

2.4 For the aforementioned reasons, the proprietor of the patent can therefore in no way be accused of behaviour contrary to “ordre public” or morality under Article 53(a) of the EPC, based on filing of the patent application and patenting the claimed process for the production of a *Pelargonium sidoides* and/or *Pelargonium reniforme* extract. The statements made by Opponent 02 to this effect are therefore totally off the mark.

2.5 The submission of Opponent 02 relating to EPC Article 53(b) are as fallacious and totally beside the point with respect to patent law. This is most clearly shown by the assertions in Section 5 on Pages 4 and 5 of the written submission of opposition that the claimed process for the production of an extract from *Pelargonium sidoides* and/or *Pelargonium reniforme* would lead to a legal monopoly over the two types of plants themselves.

A brief note to the benefit of the layman in patent law: the process claims in the patent in-suit protect solely the specifically claimed process for the production of an extract from *Pelargonium sidoides* and/or *Pelargonium reniforme* and the product of that process obtained immediately thereafter, i.e. the extract obtained immediately after this (and exclusively after this) process (Article 64(2), EPC). It is therefore not necessary to further discuss the submission by Opponent 02 in this regard with respect to patent law.

2.6 To summarise, the proprietor of the patent wishes to emphasise that he is well aware of his social and moral obligations as set out by the Convention on Biological Diversity and that he is following these conscientiously.

- The proprietor of the patent explicitly refers to the geographic origin of *Pelargonium sidoides* in his patent specifications.

- *Pelargonium sidoides* is exported on the basis of official collection and export permits.

- The proprietor of the patent supports the indigenous population through the creation of steady and substantial income, by generating know-how and sustainable income in South Africa through controlled cultivation and through cooperative research projects with South African partners.

- The proprietor of the patent in addition monitors the sustainability of his operations through commissioning of independent surveys monitoring the Pelargonium populations and monitoring the socio-economic effect of collecting Pelargonium in the wild. In this respect, the results of the third survey, which confirms the sustainability of collecting in the wild, are now available.

All of the above shows that this procedure is highly inappropriate as a vehicle for criticising the proprietor of the patent with respect to the Convention on Biological Diversity. The proprietor of the patent on the contrary considers himself closely associated with the people in South Africa and Lesotho, who have a steady and sustainable income and benefit from the transfer of know-how to South Africa and Lesotho as a result of his activities.

Irrespective of the fact that the proprietor of the patent anyhow complies with the criteria of the Convention on Biological Diversity, it must be pointed out that this fact is of no legal relevance to the legality of the awarded European patent in this patent opposition procedure.

And finally, the proprietor of the patent cannot be accused, either on legal or moral grounds, of not complying with the provisions of the Convention on Biological Diversity if the content and specific realisation of these provisions were only concretised years after the date of filing of the patent, as in the regulation for access to and benefit sharing of biological resources which came into force in South Africa only from 1 April 2008. This carries even more weight considering that the proprietor of the patent has in the past complied with the provisions of the CBD far beyond the legal requirements.

III. Novelty (Article 54, EPC)

1. Objection of lack of novelty by Opponent 01

   In his written submission of opposition, Opponent 01 does not differentiate between the questions of novelty and inventive steps and it is not evident from which prior art described in the documents the claimed process in accordance with the granted patent in-suit and particularly under Claim 1 of this main request can be directly and obviously deduced.

   None of documents D1 to D7 cited by Opponent 01 directly and obviously exhibit all the characteristics of the independent process claim 1, both under the granted patent in-suit and also under the main request.

2. Objection of lack of novelty by Opponent 02

   Opponent 02 also fails to consider the standard of the European Patent Office for examination for novelty. He also refers to documents D1 and D2 of the proceedings for grant (documents D3 and D24 in the opposition procedure), the content of which had been recognised at length in the proceedings for grant already. None of these two documents directly and obviously discloses the claimed process under discussion here.

With respect to the novelty, Opponent 02 refers to the two cited decisions **G 2/88** and **G 1/92** of the Enlarged Board of Appeal.

In connection with the discussion by Opponent 02 of the two decisions **G 2/88** and **G 1/92** of the Enlarged Board of Appeal, we refer to the explanations in the proceedings for grant and in particular to the submission dated 11 January 2007, where the following is stated with respect to the content of documents D1 and D2:

> *"…documents D1 and D2, both relating to the Umckaloabo® phyto-therapeutic agent, an ethanolic fluid extract from the Pelargonium sidoides and/or reniforme root which has for years been successfully deployed in the therapy of respiratory and HNO infections.*
>
> *Neither document D1 nor D2, however, describe a process for the production of a Pelargonium sidoides and/or Pelargonium reniforme extract. The claimed process was therefore publicly disclosed neither in document D1 nor in document D2.*
>
> *Pursuant to the adjudication of the Boards of Appeal and the Enlarged Board of Appeal of the European Patent Office, it is also not permissible to contend that a certain document inherently discloses the claimed invention and is therefore prejudicial to novelty. Decision G2/88 emphasises that the decision shall be made based on what has been made available to the public, not on what may be inherently contained in what has been made available to the public.*
>
> *This means that the reference to Umckaloabo® in documents D1 and D2 as an ethanolic fluid extract is in no way prejudicial to the novelty of the special process described in Claim 1 for the production of Pelargonium sidoides and/or reniforme extracts.*

> *"It was furthermore explained in the G1/92 statement that a product that is available in the trade does not actually disclose anything beyond its composition or internal structure;* refer to adjudication of the Board of Appeal of the European Patent Office, 4th edition 2001, Section 2.4, Page 68.
>
> *The novelty of the claimed process with respect to the disclosure of an ethanolic fluid extract in documents D1 and D2 should therefore be accepted."*

It is also incomprehensible in what sense the claimed process could directly and obviously be extracted from the other two documents D8 and D9 cited by Opponent 02.

The authors of D8 did not even have the plant material at their disposal, as is evident from the first paragraph on Page 37 of D8:

> *"we have never seen it [the "Umckaloabo" plant], as we have never been able to obtain a sample from Mr. Stevens."*

Annexure D8 dates back to 1930 and contains no descriptions of a process for producing an extract, even less the special process steps described in Claim 1 of the patent in-suit or main request. In addition, only alcohol is named in connection with the liquid extract described on Page 39, without specifying the type of alcohol referred to.

From D9, on the other hand, it is clear that methanolic extracts were used there. D9 is mentioned in Paragraph [0006] of the patent in-suit, with a note that this document describes the production of an extract using the Soxhlet method and pure methanol. The full alcohol extraction of the drug described on Page 292 under the heading of "Thin film chromatography" therefore clearly refers to a full methanol extraction. In this respect, the experimental part on Page 295 of Annexure D9 is referred to in particular. The extraction agent referred to there is exclusively methanol. In method B, for instance, the drug is Soxhlet extracted under reflux in methanol for five hours.

How, and with what solvents the percolate described there was produced is therefore not clear either from the statement on Page 294, which was also cited by Opponent 02.

None of the cited documents are therefore directly and obviously prejudicial to the novelty of the claimed process.

3. Objection of lack of novelty by Opponent 03

Opponent 03 refers to documents D15 and D16 in his objection of lack of novelty. Opponent 03 in this context holds that the content of D15 and D16 must be seen in combination.

Irrespective of the question whether it is admissible in this procedure to combine the content of the two documents D15 and D16 to judge the novelty of the process claimed in the patent in-suit (which is contested here), the novelty of the claimed process pursuant to the main request should be accepted for such reason already that there is no disclosure of the mashing with a diluted ethanolic solvent before percolation, whereby mashing and percolation are performed with different concentrations of aqueous ethanol in the specified weighted average concentration. The two-step maceration with 10-92 % ethanol by weight is also not disclosed.

The prescription 4a in Annexure D16 refers to mother tinctures and liquid dilutions.

> *"Mother tinctures according to prescription 4a are produced in accordance with the procedure for maceration or percolation using 1 part drug and 10 parts ethanol of suitable concentration (unless prescribed in the monograph) as described in the TINCTURES monograph of the Pharmacopoeia."*

In connection with *Pelargonium sidoides* and/or *reniforme* D16, however, merely describes “maceration or percolation”, with the detail limited to the above citation.

Therefore D15, even in combination with D16, does not directly and obviously disclose the claimed process pursuant to the main request.

4. Objection of lack of novelty by Opponent 04

With reference to Annexure D25, Opponent 04 questions the novelty of the claimed process.

Annexure D25 refers to the Red List and the Umckaloabo® or Umckaloabo Stevenskur® medicinal product. A percolate 1:10 of Rad. Umckaloabo (Geraniaceae) is described there, with the note that the medicinal product contains ethanol.

This document therefore also does not directly and obviously disclose the special extraction method described in Claim 1 of the main request, where the percolation is preceded by mashing and this mashing and percolating is performed with different concentrations of aqueous ethanol. Also refer to the preceding discussion of decisions **G 2/88** and **G 1/92** in Section 2 in this respect.

IV. Inventive step (Article 56 EPC)

1. Opponent 01

As explained before in Section III., Opponent 01 does not clearly differentiate between the aspects of novelty and inventive step in his written submission of opposition.

Documents D1 and D2 referred to by Opponent 01 appear unsuitable as the basis for assessing the inventive step, since they deal with the production of extracts from plant material in a very general way only, without either of the two documents turning to *Pelargonium sidoides* and/or *Pelargonium reniforme*.

Document D1 states on Page 210, left hand column, second last paragraph, that there are many known extraction methods, the selection of which depends on the nature of the plant material and the compounds to be isolated ("a variety of methods are available for extraction and the choice depends on the nature of the plant material and the compounds to be isolated."). But *Pelargonium sidoides* and/or *reniforme* are not mentioned in the list of examples of plant material on Page 210, right hand column, lines 1-3.

Correspondingly, document D2 also discloses maceration and percolation in a very general way as examples of solvent extraction methods, together with water vapour distillation. This document also does not address any details about extraction from *Pelargonium sidoides* and/or *reniforme* roots. But this document also states that there is no single perfect method and that the advantages and disadvantages must be balanced against each other ("there is no single perfect method and so the advantages and disadvantages of each must be evaluated"; see Page 15, bottom.)

It is also not evident from prior art that, with reference to *Pelargonium sidoides* and/or *reniforme* roots, only solvent extraction methods appear suitable and that in this respect only aqueous ethanol appears suitable as solvent for the production of the extract. On the contrary, known prior art that actually deals with the production of *Pelargonium sidoides*/*reniforme* extracts advises against the use of (aqueous) ethanol as the extraction agent and proposes acetone/water, methanol and water as the extraction agent; refer Paragraph [0006] of the patent in-suit.

Opponent 01 further argues that it is clearly obvious from documents D3, D4 and D5 that cumarins represent the class of relevant compounds that are to be extracted from *Pelargonium sidoides* and/or *Pelargonium reniforme*. These documents state that the cumarins are the main active biological ingredients.

But this contradicts the results obtained in accordance with the invention, which indicate that the contribution of cumarins to the antioxidative effect is insignificant, since the total cumarin content in the extracts is virtually constant, independent of the process and solvent; refer Paragraph [0012] of the patent in-suit.

Since the total cumarin contents are thus of little significance in accordance with the invention, the polarity of the solvent is not decisive with respect to the choice of extraction solvent, contradicting the explanations of Opponent 01 on Page 5, third paragraph.

Documents D3, D4 and D5 dealing, among other, with the Umckaloabo® product, cannot suggest the claimed special maceration or percolation process under Claim 1 of the main request.

None of these documents gives any indication of the process claimed in accordance with the invention. Those documents refer only to the Umckaloabo® product, which is an ethanolic fluid extract (D3, Page 144, left hand column, second paragraph) or an ethanolic extract of the buried parts of *Pelargonium reniforme Curt.* and *P. sidoides DC.* (D4, summary) or a fluid extract (see D5, Page 165, left hand column, first paragraph).

Opponent 01 finally also refers to document D7, particularly the process claims 1 and 2.

The process for the production of low-pesticide active agent concentrates from plants described there bears no relation, however, to the special maceration or percolation process claimed in accordance with the invention and is also not capable of challenging the inventive step with respect to the claimed subject matter.

To summarise, it can be recorded that none of the documents cited by Opponent 01 suggests the special maceration or percolation process of *Pelargonium sidoides* and/or *reniforme* roots as claimed in accordance with the invention.

2. Opponent 02

As already explained with respect to the question of novelty, the criterion applied by Opponent 02 for judging the existence of an inventive step is also not in agreement with established practice and particularly not in agreement with the "problem-and-solution-approach" developed by the Board of Appeal of the European Patent Office to assess the inventive step requirement.

In the opinion of Opponent 02, the number of intellectual steps is an important criterion in the assessment of the inventive level. In this respect, Opponent 02 refers to an article in GRUR Int. dated 1978. As is well-known, the European Patent Office started its activities in 1978 and, as described above already, the test for inventive steps has since developed in a completely different direction, viz. towards the "problem-and-solution-approach".

The "problem-and-solution-approach" has a three-phase structure:

i) Determining the "closest prior art",

ii) Establishing the "objective technical problem" to be solved and

iii) considering whether or not the claimed invention, starting from the closest prior art and the objective technical problem, would have been obvious to the skilled person; refer Guidelines, C-IV, 11.7.

The remainder of the explanations in this respect by Opponent 02, for the determination of the inventive step in accordance with the "multi-step method", are therefore besides the point.

It can also not be established whether any of the documents cited by Opponent 02 would be suitable for referencing as closest prior art in considering an inventive step pursuant to the problem-and-solution-approach.

The closest prior art would constitute the combination of characteristics, disclosed in a single source, representing the most promising point of departure for an obvious development leading to the claimed invention. In practice, the closest prior art is generally that which corresponds with a similar purpose of use and which requires the least structural and functional modifications to match the claimed invention.

The closest prior art shall be assessed by the opinion of a skilled person on the day preceding the effective date of filing or priority for the claimed invention.

In determining the closest prior art, the information provided by the applicant himself as known in his description and patent claims, must be considered; refer Guidelines C-IV, 11.7.1.

The invention underlying the patent in-suit concerns a process for the production of *Pelargonium sidoides* and/or *Pelargonium reniforme* extracts.

Therefore, the only documents suitable as closest prior art are those discussing a process for the production of *Pelargonium sidoides* and/or *Pelargonium reniforme* extracts.

In this respect, the patent specification refers to various known prior art methods in Paragraph [0006]. In prior art, extracts from the *Pelargonium sidoides* and/or *reniforme* roots were generally produced, for instance, by simple maceration using acetone/water 4/1 (Kayser, O., Kolodziej, H., Phytochemistry 39, 1181-1185 (1995)) or pure methanol using the Soxhlet method (D9). Pure aqueous extracts were also used (D3) for therapeutic purposes. An ethanolic extract of *Pelargonium reniforme*/*sidoides*, diluted with glycerine, is available in the trade (Red List 2001).

None of these four documents deals with an extraction method using aqueous ethanol as a solvent. More specifically, none of these documents deals with a two-step maceration process or a *Pelargonium sidoides* and/or *reniforme* percolation process preceded by mashing.

The Umckaloabo® product is the only one referring to an ethanolic extraction, but the process for producing the ethanolic extraction is not described anywhere in the prior art.

Since, therefore, no closest prior art is evident in the opposition procedure other than the one already described in the specifications of the patent in-suit in Paragraph [0006], the task named in Paragraph [0008] also refers to the task of finding the objective technical problem pursuant to the problem-and-solution-approach. It is the purpose of this invention, therefore, to provide an improved, gentle method for the production of *Pelargonium sidoides* and *Pelargonium reniforme* extracts, with a higher yield of extracts and with simultaneously also improving the effect of the extracts.

The fact that this task has been achieved with the process claimed in accordance with the invention has already been explained in detail in the introduction in Section I., 4. above.

The third phase of the “problem-and-solution-approach” requires investigation as to whether there is a principle in prior art overall which would (not just could, but would) lead the skilled person dealing with the objective technical problem to change or adapt the closest prior art and thereby arrive at something which would fall under the patent claim, to achieve that which is achieved through the invention.

In other words, the intention is not to establish whether the skilled person could have arrived at the invention by changing or adapting the closest prior art, but to establish whether he would have actually arrived there because prior art prompts him to, in the hope of thereby solving the objective technical problem, or in the expectation of an improvement or advantage; refer Guidelines C-IV, 11.7.3.

The explanations of Opponent 02 with respect to the question of inventive step deal only with the question of what the average skilled person could have done, but not with the only question that is relevant, i.e. whether the average skilled person would have arrived at the process claimed in accordance with the invention because prior art prompted him to, in the hope of thereby solving the objective technical problem, or in the expectation of making an improvement or gaining an advantage.

Opponent 02 (and the other opponents also) neglected to explain how the average skilled person would be prompted to solve the underlying technical problem by applying the claimed special percolation process after first mashing with aqueous ethanol in a specific range of concentrations, or the two-step maceration process with the use of 10-92 % ethanol by weight.

Merely the fact that maceration and percolation, among other, were known as extraction methods would not prompt the average skilled person to modify the different prior art processes using different solvents in a way that would lead to the process claimed in accordance with the invention.

The argument of Opponent 02 is furthermore based on a classic impermissible retrospective approach, starting from the knowledge of this invention.

This is evident, among other, from Annexure D14, the sworn statement by Milile Rwexu. This sworn statement exclusively deals with the production of an aqueous extract and therefore in no way addresses the production of an aqueous-ethanolic extract as described in the process in accordance with the invention. Opponent 02 could not, without knowledge of this invention, propose in Section 2, on Page 10 of his written submission of opposition, that the cold water merely required the addition of ethanol. It may be true that the average skilled person simply needed to add ethanol to the cold water, but this does not comply with the standard test for inventive steps. The question should rather be: what would prompt the skilled person dealing with the objective technical problem to add ethanol to the cold water in order to solve the technical problem? The proprietor of the patent does not deny that pure aqueous extracts have also been used for therapeutic application already in prior art, and in this respect again refers to Paragraph [0006] of the patent in-suit and document D3 cited there.

In addition, it remains to be stated that the addition of ethanol alone to the cold water does not lead to the claimed process in the patent in-suit, which describes a specific maceration or percolation process using a specific solvent at a defined concentration.

3. Opponent 03

The arguments put forward by Opponent 03 in addressing the question of the inventive step also does not comply with the problem-and-solution-approach. The general discussion is rather around the known prior art, without clearly indicating a closest prior art on the basis of which the inventive step should be judged by applying the problem-and-solution-approach – thereby also failing to clearly indicate the objective technical problem. The arguments put forward by Opponent 03 also do not comply with the standard test for the inventive step in the third phase of the "problem-and-solution-approach", which requires us to investigate whether there is a principle in prior art overall which would (not just could, but would) lead the skilled person dealing with the objective technical problem to change or adapt the closest prior art, considering this principle, and thereby arrive at something which would fall under the patent claim, to achieve that which is achieved through the invention; refer to the above detailed discussion of the problem-and-solution-approach in Section 2.

Opponent 03 puts forward the following arguments in connection with the characteristics of the granted Claims 4 and 5 which are now included in Claim 1 of the main request:

> *"The use of different concentrations of ethanol for mashing and percolation under Claim 4 is obvious to the skilled person, since the processes are different from each other and because he would obviously choose a suitable concentration for each process."*
>
> *"The additional characteristic in Claim 7 is not inventive either for the same reasons as in Claims 5 and 6."*

Referring to Claims 5 and 6, Opponent 03 puts forward the following, among other:

> *"The limitation to 10-60% is also not based on an effect shown in the description as solving a problem, but is an arbitrarily selected range and therefore not inventive."*

Opponent 03 has therefore not submitted anything on the question of what would prompt the skilled person dealing with the objective technical problem to use different concentrations of ethanol for mashing and percolating, whereby the weighted average concentration of the aqueous ethanol used for mashing and percolating lies in the range of 10-92 % by weight. This is analogously also applicable to the claimed two-step maceration with 10-92 % ethanol by weight.

It has previously already been explained in the introductory Section I., 4. that, in accordance with this specific extraction method under Claim 1 of the main request, an unexpectedly improved extract is obtained, with a higher yield.

In this respect it bears mentioning that, even when the objective technical problem is formulated as the provision of an alternative process for the production of a *Pelargonium sidoides* and/or *Pelargonium reniforme* extract, i.e. if the surprisingly favourable properties of the obtained extract are ignored, the claimed process in accordance with the main application meets the inventive step requirement, since it does not obviously follow from the cited prior art. None of the cited prior art documents proposes to provide a process for the production of a *Pelargonium sidoides and/or Pelargonium reniforme* extract by percolation using different concentrations of aqueous ethanol for mashing and percolating, whereby the weighted average concentration of the aqueous ethanol used for mashing and percolating lies in the range of 10-92 % by weight, or to macerate using a two-step maceration with 10-92 % ethanol by weight.

The argument put forward by Opponent 03 can therefore not challenge the existence of an inventive step for the claimed subject matter either.

4. Opponent 04

Opponent 04 attempts to challenge the existence of an inventive step, based on documents D3 and D24 as the closest prior art.

Opponent 04 argues that it is the purpose of the patent in-suit to improve the extraction method and to achieve better yields, based on the D3 and D24 extracts.

In the discussion of the existence of an inventive step according to the third phase of the problem-and-solution-approach, Opponent 04 argues, with reference to the characteristics of the granted Claim 4 which have now been incorporated into the main claim of the main request, that mashing and percolating with different concentrations of aqueous ethanol is an obvious variant without any proven advantages. In connection with the characteristics of the granted Claims 7 and 8, Opponent 04 also argues that the weighted average concentrations in the region of 10-60 % by weight of the aqueous ethanol used for mashing and percolation are merely conventional concentrations and that it has not been shown that there are surprising advantages for the embodiment where the concentrations are 35 % ethanol and 5 % ethanol by weight for mashing and percolating respectively, in a 2:8 ratio.

Therefore, Opponent 04 also does not provide any reasons why the average skilled person has been prompted to select specifically this process variant which is now claimed in the main request, in the hope of solving the objective technical problem.

In addition, the examples in the patent in-suit are proof of a surprisingly advantageous effect of the claimed process, refer Section 1.4, supra.

To summarise, it is therefore recorded that the arguments put forward by Opponent 04 also cannot challenge the existence of an inventive step for the claimed subject matter.

V. Feasibility of the invention (Article 83 EPC)

With respect to the embodiment under Claim 8, Opponent 01 argues that this has not been adequately disclosed for an average skilled person to implement; refer third paragraph on Page 6 of Opponent 01's written submission of opposition.

In a glaring contradiction, Opponent 01 simultaneously argues, in the immediately preceding paragraph on the same page, that the embodiments under Claims 2 to 8 are general knowledge and therefore neither new nor inventive.

In response to this objection under Article 83 EPC to the embodiment under Claim 8 of the granted patent, example 1 of the patent in-suit is referred to. Referring to this, the average skilled person may also obtain an example of a suitable ratio between drug and solvent, rendering the objection of Opponent 01 on Page 6, fifth paragraph, baseless.

In the fourth paragraph on Page 6 of the written submission of opposition by Opponent 01, the latter states that it is not "clear" what the meaning is of the "2:8" ratio in Claim 8 and why the ratio is not specified as "1:4".

The answer is simply that it is easier to divide by 10 and that there is no other difference. In this context, Paragraph [0009] lines 48-50 of the patent in-suit are referred to, where an example of the calculation for an average weighted concentration of the solvent is given.

Finally, Opponent 02 also raises a half-hearted objection under Article 83 EPC, in which it is clear already in the heading on Page 5 of his written submission of opposition that the objection is an objection under the clarity requirement pursuant to Article 84 EPC. Since Article 84 EPC is not a ground for opposition, it is only pointed out briefly here that Opponent 02 himself, with the detailed analysis of characteristics on Page 6, directly rebuts this objection on Page 5 of his written submission of opposition.

VI. Summary

The subject matter of the aforementioned claims under the main request is new and inventive for the aforementioned reasons. The claimed process does not directly and obviously follow from any of the cited prior art documents and, in addition, there is no teaching overall in the cited prior art that would (not just could, but would) prompt the skilled person dealing with the objective technical problem to change or adapt the closest prior art, considering this teaching, and thereby arriving at something falling under the claimed subject matter, in order to achieve what this invention achieves. It is also irrelevant in this context whether the objective task is formulated as provision of an improved or an alternative process.The arguments of the opponents anyhow only deal with the question whether the skilled person, by changing or adapting the closest prior art, could have arrived at the invention and ignore the one and only decisive question of whether he actually would have arrived there because prior art prompted him to. But most of the opponents in any event neglected to follow the problem-and-solution-approach for testing for inventive step, as developed by the Boards of Appeal of the European Patent Office.

The disclosure of the claimed invention is also adequate for the average skilled person to follow without a problem.

Finally, there is also no exception to patentability pursuant to Article 53 a) or b) EPC.

The patent in-suit should for this reason be maintained to the full extent of the main request and the notices of opposition be rejected.

Dr. Holger Adam

Professional representative

Annexures

Copy of Claims 1 to 5 under the main request

D32: Tade Matthias Spranger, “Indigene Völker, 'Biopiraterie' und Internationales Patentrecht”, GRUR 2001, Pages 89-92

D33: T. Brendler, B.-E. Van Wyk, J. Ethnopharmacol., 119 (2008) 420-433