

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent of )  
Bengt ÅGERUP )  
Patent No. 5,827,937 )  
Issued: October 27, 1998 )  
FOR: POLYSACCHARIDE GEL )  
COMPOSITION )

MAIL STOP: PATENT EXTENSION

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**TRANSMITTAL LETTER FOR APPLICATION FOR EXTENSION  
OF PATENT TERM UNDER 35 U.S.C. § 156**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Enclosed is an Application for Extension of Patent Term Under 35 U.S.C. § 156 (an original and three copies) for the above-identified patent.

Also enclosed with the original and each of the three copies are the following documents:

1. Attachment A (Copy of Product Information About RESTYLANE® Injectable Gel)
2. Attachment B (Copy of Approval Letter from the FDA for RESTYLANE® Injectable Gel)
3. Attachment C (Copy of U.S. Patent No. 5,827,937)
4. Attachment D (Copy of Statutory Disclaimer of Claim 4 for U.S. Patent No. 5,827,937)
5. Attachment E (Copies of Maintenance Fee Statement for U.S. Patent No. 5,827,937)
6. Attachment F (Copy of Recorded Assignment Document for U.S. Patent No. 5,827,937)
7. Attachment G (Copy of Authorization from Q-MED Scandinavia to Q-MED AB to Rely Upon Activities of Q-MED Scandinavia Before the FDA in Making Its Applications for Extension and Extension of Patent Term)

COPY

APP 1

8. Attachment H (Copy of Power of Attorney).

COPY

Please charge the requisite fee in the amount of \$1,120.00 to Deposit Account No. 02-4800.

The Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit account No. 02-4800. This paper is submitted in duplicate.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, LLP



Benton S. Duffett, Jr.  
Registration No. 22,030

P.O. Box 1404  
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Date: February 10, 2004

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

*In re* Patent of ) **MAIL STOP: PATENT EXTENSION**  
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Bengt ÅGERUP )  
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**APPLICATION FOR EXTENSION OF  
PATENT TERM UNDER 35 U.S.C. § 156**

**MAIL STOP: PATENT EXTENSION**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In accordance with the provisions of 35 U.S.C. § 156 and 37 C.F.R. § 1.710 *et seq.*, the owner of record of U.S. Patent No. 5,827,937 requests that the term of this patent be extended by **879 days** to expire on **December 12, 2017**.

U.S. Patent No. 5,827,937 was filed on July 17, 1995 and issued on October 27, 1998 for "POLYSACCHARIDE GEL COMPOSITION," listing Bengt Ågerup as the sole inventor. The term of U.S. Patent No. 5,827,937 will expire, unless extended, on July 17, 2015 (*i.e.*, twenty years from the date on which the application for the patent was filed in the United States).

Application For Extension Of  
Patent Term Under 35 U.S.C. § 156  
for U.S. Patent No. 5,827,937  
Attorney Docket No.: 003300-356

Q-MED AB, a Swedish corporation, is the assignee of the entire right, title and interest in U.S. Patent No. 5,827,937, granted to Bengt Ågerup, on October 27, 1998 for POLYSACCHARIDE GEL COMPOSITION, by virtue of an assignment from the inventors to Q-MED AB, Upsala, Sweden, recorded on September 8, 1997 at Reel 8741, Frame 0942.

Q-MED AB submits this application for extension of the patent term of U.S. Patent No. 5,827,937 by providing the following information in accordance with 35 U.S.C. § 156 and 37 C.F.R. § 1.710 *et seq.*, and follows the numerical format set forth in 37 C.F.R. §1.740(a)(1)-(15)

**(1) COMPLETE IDENTIFICATION OF PRODUCT**

The product presently subject to regulatory review is RESTYLANE® Injectable Gel (trade name). Product information from the U.S. Food and Drug Administration website regarding RESTYLANE® Injectable Gel is attached at ATTACHMENT A.

RESTYLANE® Injectable Gel contains 20 mg/ml of non-animal stabilized hyaluronic acid (hereinafter “NASHA”) in buffered physiological sodium chloride solution pH 7. RESTYLANE® Injectable Gel is a sterile, transparent, viscous gel supplied in a 1 ml disposable glass syringe filled with 0.4 or 0.7 ml gel. The syringe is equipped with a tip cap, finger grip, plunger stopper and plunger rod. The product is for single use only. A sterile 30G needle is supplied in the package.

Hyaluronic acid is a polymer containing alternating units of glucuronic acid (GlcUA) and N-acetylglucosamine (GlcNAc). NASHA is a generic name for the stabilized forms of Hyaluronic Acid (hereinafter “HA”) from Q-MED. The HA in RESTYLANE® Injectable Gel is stabilized by adding a minimum amount of 1,4-butanediol diglycidyl ether to allow formation of a 3-dimensional HA molecular network (gel). The patented chemical stabilizing process used by Q-MED does not change the polyanionic character of the polysaccharide chain. As only about 1% of the polysaccharide has been stabilized the substance remains biocompatible.

Hyaluronic acid belongs to a group of very few substances, which are identical in all living organisms. It is a natural polysaccharide that is present throughout the tissues of the body.

It occurs as an important structural element in the skin and in subcutaneous and connective tissues as well as in the synovial tissue and fluid. RESTYLANE® Injectable Gel is biologically almost identical to hyaluronic acid and is degraded in the body by the same metabolic pathway as endogenous hyaluronic acid. RESTYLANE® Injectable Gel acts by adding volume to the tissue, thereby restoring the skin contours to the desired level of correction. RESTYLANE® Injectable Gel is naturally integrated into the tissue and will in time undergo isovolemic degradation.

Application For Extension Of  
Patent Term Under 35 U.S.C. § 156  
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Attorney Docket No.: 003300-356

**(2) IDENTIFICATION OF FEDERAL STATUTE/PROVISION OF LAW**

RESTYLANE® Injectable Gel is subject to regulatory review under Section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355), as a Class III medical device.

Application For Extension Of  
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**(3) DATE ON WHICH PRODUCT RECEIVED PERMISSION FOR COMMERCIAL  
MARKETING OR USE**

RESTYLANE® Injectable Gel received permission for commercial marketing under  
Section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355) on **December 12,  
2003**. A copy of the approval letter is attached as ATTACHMENT B.

**(4) IDENTIFICATION OF EACH ACTIVE INGREDIENT**

37 C.F.R. §1.740(a)(4) requires that in the case of a drug product, “an identification of each active ingredient in the product and as to each active ingredient, a statement that it has not been previously approved for commercial marketing or use under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act, or a statement of when the active ingredient was approved for commercial marketing or use (either alone or in combination with other active ingredients), the use for which it was approved, and the provision of law under which it was approved.”

RESTYLANE® Injectable Gel is a Class III medical device, not a drug product. Moreover, RESTYLANE® Injectable Gel does not contain any active ingredient. Accordingly, this section is not applicable.

**(5) TIME PERIOD FOR SUBMITTING APPLICATION**

This application is being submitted within the sixty day period permitted for submission pursuant to § 1.720(f). Specifically, this application is being submitted within the sixty-day period “beginning on the date the product first received permission for commercial marketing or use under the provisions of law under which the applicable regulatory review period occurred.”

RESTYLANE® Injectable Gel received permission for commercial marketing under Section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355) on **December 12, 2003**. A copy of the approval letter is attached at ATTACHEMENT B. Sixty days from December 12, 2003 would be February 10, 2004.

Thus, the last day on which this application could be submitted is **February 10, 2004**.

**(6) IDENTIFICATION OF PATENT**

The patent for which patent term extension is being sought is U.S. Patent No. 5,827,937, which was filed on July 17, 1995 and issued on October 27, 1998 for “POLYSACCHARIDE GEL COMPOSITION,” listing Bengt Ågerup as the sole inventor.

The term of U.S. Patent No. 5,827,937 will expire, unless extended, on July 17, 2015 (twenty years from the date on which the application for the patent was filed in the United States).

Application For Extension Of  
Patent Term Under 35 U.S.C. § 156  
for U.S. Patent No. 5,827,937  
Attorney Docket No.: 003300-356

**(7) COPY OF PATENT**

A copy of U.S. Patent No. 5,827,937 is attached as ATTACHMENT C.

**(8) OTHER PATENT DOCUMENTS**

A copy of the statutory disclaimer of Claim 4 is attached as ATTACHMENT D.

The records of the undersigned do not indicate that any other disclaimer, certificate of correction or reexamination certificate were issued in U.S. Patent No. 5,827,937.

The fourth-year maintenance fee has been paid, and a copy of the maintenance fee statement (from the U.S. Patent & Trademark Office Web site) verifying the payment is attached as ATTACHMENT E.

A copy of the recorded Assignment documents (from the records of the U.S. Patent and Trademark Office) are attached as ATTACHMENT F.

**(9) CLAIM(S) COVERING THE PRODUCT**

The claims of U.S. Patent No. 5,827,937 cover the approved product, RESTYLANE® Injectable Gel, as well as a method of manufacturing the approved product.

As required, Applicants provide a showing below, which lists each applicable patent claim and demonstrates the manner in which each of the following claims reads upon the approved product and the method of manufacturing the approved product.

<i>Claim as-issued</i>	<i>RESTYLANE® Injectable Gel</i>
<p>1. A process for preparing a cross-linked biocompatible polysaccharide gel composition, which process comprises the following steps:</p> <p>(i) forming an aqueous solution of a water soluble, cross-linkable polysaccharide;</p> <p>(ii) initiating a first cross-linking reaction whereby cross-linking of said polysaccharide is effected using a polyfunctional cross-linking agent therefor;</p>	<p>RESTYLANE® Injectable Gel is a cross-linked biocompatible polysaccharide gel composition.</p> <p>RESTYLANE® Injectable Gel is manufactured by a process whereby hyaluronic acid prepared by fermentation of Streptococcus is first dissolved in an alkaline aqueous solution. Hyaluronic acid is a “a water soluble, cross-linkable polysaccharide.”</p> <p>A cross-linking agent, 1,4-butanediol diglycidyl ether, is used to initiate a first cross-linking reaction. Thus, cross linking of the polysaccharide is effected using “a polyfunctional cross-linking agent.” (See, e.g., column 4, lines 10-21 of U.S. Patent No. 5,827,937 for the</p>

<i>Claim as-issued</i>	<i>RESTYLANE® Injectable Gel</i>
<p>(iii) sterically hindering the first cross-linking reaction such that it is terminated before gelation occurs, resulting in the production of an activated polysaccharide;            and</p> <p>(iv) performing a second cross-linking reaction after sterically unhindered conditions are reintroduced for said activated polysaccharide to produce a viscoelastic gel.</p>	<p>definition of polyfunctional cross-linking agent.)</p> <p>The above solution was first incubated and then diluted in a physiological buffer and neutralized. The dilution step accomplishes the step of “sterically hindering the first cross-linking reaction such that it is terminated before gelation occurs, resulting in the production of an activated polysaccharide,” as recited in the claims. (<i>See, e.g.</i>, column 3, lines 25-31 of U.S. Patent No. 5,827,937.)</p> <p>The activated polysaccharide was then rotary evaporated to form a viscoelastic gel with a neutral pH and a HA concentration of about 2% (w/w). The rotary evaporation step accomplishes the step of “performing a second cross-linking reaction after sterically unhindered conditions are reintroduced for said activated polysaccharide to produce a viscoelastic gel.” (<i>See, e.g.</i>, column 3, lines 32-56 of U.S. Patent No. 5,827,937.)</p> <p>Thus, Claim 1 reads on the method of manufacture for RESTYLANE® Injectable Gel.</p>
<p>2. A process according to claim 1, wherein the polysaccharide is selected</p>	<p>RESTYLANE® Injectable Gel comprises a cross-linked gel of hyaluronic acid.</p>

<i>Claim as-issued</i>	<i>RESTYLANE® Injectable Gel</i>
from the group consisting of glucose amino glucans.	Hyaluronic acid is a polysaccharide that is a “glucose amino glucan.” Thus, Claim 2 reads on the method of manufacture for RESTYLANE® Injectable Gel.
3. A process according to claim 2, wherein said glucose amine glucan comprises hyaluronic acid.	RESTYLANE® Injectable Gel comprises a cross-linked gel of hyaluronic acid, which is a glucose amine glucan. Thus, Claim 3 reads on the method of manufacture for RESTYLANE® Injectable Gel.
5. A process according to claim 4, wherein said glycidyl ether comprises 1,4-butanediol diglycidylether.	RESTYLANE® Injectable Gel uses a glycidyl ether, which comprises 1,4-butanediol diglycidylether. Thus, Claim 5 reads on the method of manufacture for RESTYLANE® Injectable Gel.
6. A process according to claim 1, wherein said sterically hindering of the cross-linking reaction comprises diluting the aqueous medium in which the cross-linking reaction is performed, to accomplish a lower concentration of the polysaccharide in said medium.	As discussed above, the manufacture of RESTYLANE® Injectable Gel comprises a “cross-linking reaction” that includes “diluting the aqueous medium in which the cross-linking reaction is performed, to accomplish a lower concentration of the polysaccharide in said medium.” Thus, Claim 6 reads on the method of manufacture for RESTYLANE® Injectable Gel.
7. A process according to claim 1, wherein said reintroduction of sterically unhindered conditions comprises evaporating the aqueous medium in which	The manufacture of RESTYLANE® Injectable Gel comprises a “reintroduction of sterically unhindered conditions” that includes “evaporating the aqueous

<i>Claim as-issued</i>	<i>RESTYLANE® Injectable Gel</i>
the cross-linking reaction is performed, to accomplish a higher concentration of the polysaccharide in said medium.	medium in which the cross-linking reaction is performed, to accomplish a higher concentration of the polysaccharide in said medium.” Thus, Claim 7 reads on the method of manufacture for RESTYLANE® Injectable Gel.
9. A process according to claim 1, wherein the initial cross-linking reaction in the presence of a polyfunctional cross-linking agent is performed at an alkaline pH, ether cross-linking reactions thereby being promoted.	The manufacture of RESTYLANE® Injectable Gel comprises an “initial cross-linking reaction in the presence of a polyfunctional cross-linking agent” that is “performed at an alkaline pH,” with “ether cross-linking reactions thereby being promoted.” Thus, Claim 9 reads on the method of manufacture for RESTYLANE® Injectable Gel.
10. The process of claim 9, wherein the cross-linking is effected at a pH above pH 9.	The manufacture of RESTYLANE® Injectable Gel comprises a “cross-linking” reaction that is “effected at a pH above pH 9.” Thus, Claim 10 reads on the method of manufacture for RESTYLANE® Injectable Gel.
12. A process according to claim 1, wherein said sterical hindrance of the cross-linking reaction is accomplished before said cross-linking agent has been consumed.	The manufacture of RESTYLANE® Injectable Gel comprises a dilution step, which accomplishes “sterical hindrance of the cross-linking reaction.” The dilution step is “accomplished before said cross-linking agent has been consumed.” Thus, Claim 12 reads on the method of manufacture for RESTYLANE® Injectable Gel.
24. A cross-linked biocompatible	RESTYLANE® Injectable Gel is a cross-

<i>Claim as-issued</i>	<i>RESTYLANE®Injectable Gel</i>
<p>polysaccharide gel composition, which is obtainable by cross-linking of a cross-linkable polysaccharide with a polyfunctional cross-linking agent therefor in two steps,</p> <p>the first cross-linking step being terminated before gelation occurs by a sterical hindrance of the cross-linking reaction, and</p> <p>the second cross-linking step being initiated by reintroducing sterically unhindered conditions for said cross-linking reaction to continue the same up to a viscoelastic gel,</p>	<p>linked biocompatible polysaccharide gel composition, which is obtainable by cross-linking of a cross-linkable polysaccharide with a polyfunctional cross-linking agent in two steps.</p> <p>In a first step, a cross-linking agent, 1,4-butanediol diglycidyl ether, is used to initiate a first cross-linking reaction. The above solution is incubated and then diluted in a physiological buffer and neutralized. The dilution step accomplishes the step of “sterically hindering the first cross-linking reaction such that it is terminated before gelation occurs, resulting in the production of an activated polysaccharide,” as recited in the claims. (<i>See, e.g.</i>, column 3, lines 25-31 of U.S. Patent No. 5,827,937.)</p> <p>In a second step, the activated polysaccharide is then rotary evaporated to form a viscoelastic gel with a neutral pH and a HA concentration of about 2% (w/w). The rotary evaporation step accomplishes the step of “performing a second cross-linking reaction after sterically unhindered conditions are reintroduced for said activated polysaccharide to produce a viscoelastic gel.” (<i>See, e.g.</i>, column 3, lines 32-56 of U.S. Patent No. 5,827,937.)</p>

<i>Claim as-issued</i>	<i>RESTYLANE® Injectable Gel</i>
<p>wherein said gel composition exhibits retained biocompatibility, viscoelasticity and does not swell substantially when placed in contact with water.</p>	<p>RESTYLANE® Injectable Gel exhibits retained biocompatibility, viscoelasticity and does not swell substantially when placed in contact with water.</p> <p>Thus, Claim 24 reads on the method of manufacture for RESTYLANE® Injectable Gel.</p>
<p>33. A medical or prophylactic composition comprising a polysaccharide gel composition according to claim 24.</p>	<p>RESTYLANE® is a medical or prophylactic composition that comprises “a polysaccharide gel composition according to claim 24.” Thus, Claim 33 reads on the method of manufacture for RESTYLANE® Injectable Gel.</p>

**(10) RELEVANT DATES AND INFORMATION  
PURSUANT TO 35 U.S.C. § 156(g)**

The relevant dates and information pursuant to 35 U.S.C. § 156(g), and 37 C.F.R. § 1.740(a)(10)(v), to enable the Secretary of Health and Human Services to determine the applicable regulatory review period for a patent claiming a medical device are as follows:

- (a) *The effective date of the investigational device exemption (IDE) and the IDE number: IDE G990258* was submitted by Q-MED Scandinavia, Inc. on **October 14, 1999**, and became effective on August 4, 2000.
  
- (b) *The date on which the application for product approval or notice of completion of a product development protocol under section 515 of the Federal Food, Drug, and Cosmetic Act was initially submitted and the number of the application or protocol:* The application for product approval under section 515 of the Federal Food, Drug, and Cosmetic Act was initially submitted on **June 19, 2002**. The application number was **P020023**.
  
- (c) *The date on which the application was approved:* **December 12, 2003**.

**(11) BRIEF DESCRIPTION OF SIGNIFICANT ACTIVITIES**

The following is a brief description of the significant activities undertaken by the marketing applicant during the applicable regulatory review period with respect to RESTYLANE® Injectable Gel and the significant dates applicable to such activities.

<b>Date</b>	<b>To</b>	<b>From</b>	<b>Type</b>	<b>Summary</b>
March 17, 1999	FDA	Akin, Gump	Submission	Meeting request Letter Pre-IDE Meeting
October 14, 1999	FDA	A/G	Submission	Filed original IDE for treatment of cutaneous contour deformities such as nasolabial folds.
November 12, 1999	A/G	FDA	Facsimile	FDA granted conditional approval for two sites with 10 subjects each. FDA stated that issues of clinical design remain that must be addressed. Letter lists deficiencies and the protocol and RPI must be revised.
December 3, 1999	FDA	A/G	Letter	Requested a meeting with FDA to discuss clinical issues
December 15, 1999			Minutes	Safety, study design, hypersensitivity and other issues were addressed. From the minutes it appears that a formal meeting was set for January 11, 2000.
December 28, 1999				First screening visit; patient examined and received collagen test in the arm
January 6, 2000	FDA	A/G	Submission	Submission of safety data in response to questions raised in FDA's November 12, 1999 letter. This letter also refers to the December 15, 1999 conference call.
January 11, 2000			Minutes	Safety and clinical issues were discussed. FDA expects a revised protocol and

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 for U.S. Patent No. 5,827,937  
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<b>Date</b>	<b>To</b>	<b>From</b>	<b>Type</b>	<b>Summary</b>
				invited further teleconferences.
February 4, 2000	A/G	FDA	Letter	FDA acknowledged the January 6, 2000 submission and conditionally approved the IDE for 45 days but still for only 2 sites and 10 patients each. The deficiencies from the November 12, 1999 letter must be corrected.
March 16, 2000				First Patient included and treated within the study
March 16, 2000	FDA	A/G	Submission	Filed responses to FDA's November 12, 1999 letter and submitted a revised protocol (31 GE 0003) and CRF.
April 13, 2000	A/G	FDA	Letter	FDA acknowledged the March 16, 2000 submission but still only granted conditional approval. The protocol was still considered unacceptable.
April 26, 2000			Minutes	Teleconference minutes cover various protocol issues including duration, touch-up, validation of clinical endpoints, statistics, informed consent, etc.
May 11, 2000			Minutes	Teleconference
May 26, 2000	FDA	A/G	Submission	Provided FDA with revised protocol, the minutes of the May 11, 2000 teleconference, and specific responses to deficiencies.
June 9, 2000	FDA	A/G	Submission	Provided FDA with copies of various CRFs.
June 29, 2000	A/G	FDA	Letter	FDA acknowledged receipt of submissions dated May 26 and June 9 2000. Letter states the application remains conditionally approved and limited to 5 sites and 30 subjects. At issue is the validity of the clinical endpoints. FDA expects a revised protocol.

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<b>Date</b>	<b>To</b>	<b>From</b>	<b>Type</b>	<b>Summary</b>
July 6, 2000			Minutes	Minutes of a teleconference with FDA covering the June 29, 2000 letter. Call covered statistical issues.
July 7, 2000			Minutes	Minutes of a teleconference with FDA covering the June 29, 2000 letter. Call covered not statistical issues.
July 11, 2000	FDA	Buchanan Ingersoll (BI)	Submission	Submitted revised protocol, patient diaries, CRFs, example photographs in response to FDA's June 29, 2000 letter.
August 4, 2000	BI	FDA	Letter	FDA approved the IDE. FDA provided two points of advice regarding the analysis of data for safety and effectiveness.
October 12, 2000	FDA	BI	Letter	Requested that FDA allow the addition of another clinical site.
November 3, 2000	BI	FDA	Letter	FDA allowed the addition of one more clinical site.
November 14, 2000	FDA	BI	Submission	Covers manufacturing changes: scale up from 4000 to 15, 000 syringes; removed methanol from process; changed test methods and added bioburden.
December 11, 2000	BI	FDA	Letter	FDA acknowledged the November 14, 2000 letter. FDA accepted the manufacturing changes submitted.
December 12, 2000	FDA	BI	Submission	Submitted "Validation of the Wrinkle Severity Rating Scale – A Sub-study within 31 GE 0003.
January 12, 2001	BI	FDA	Letter	Submission of December 12, 2000 unacceptable. Submission only covers a 2-point scale while the protocol requires a 5-point scale. FDA requested data within 45 days of date of the letter.
January 31, 2001	FDA	BI	Fax	Sent FDA a copy of the July 6, 2000 teleconference minutes.

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<b>Date</b>	<b>To</b>	<b>From</b>	<b>Type</b>	<b>Summary</b>
February 26, 2001	FDA	BI	Submission	Submitted revised clinical validation report – see December 12, 2000 and January 12, 2001.
March 22, 2001	BI	FDA	Letter	FDA acknowledged submission of February 26, 2001. FDA accepted the revised validation report.
June 19, 2002	FDA	Q-MED	Submission	Submitted original PMA for the treatment of cutaneous contour deformities such as nasolabial folds. Also informed FDA facility ready for inspection in August 2002.
July 30, 2002	Q-MED	FDA	Letter	FDA made a threshold determination that the PMA is sufficiently complete to permit substantive review and suitable for filing. Deficiencies were noted in the letter.
September 6, 2002	FDA	Q-MED	Submission	Provided a partial response to FDA is issues listed in the July 30, 2002 FDA letter. Responds to 3 of 7 deficiencies including clinical, manufacturing, statistical areas.
September 12, 2002	FDA	Q-MED	Submission	Provided financial disclosure in and also informed FDA that some labeling would be modified per FDA’s request (July 30, 2002 letter).
October 4, 2002	Q-MED	FDA	Letter	FDA scheduled a meeting for October 10, 2002; this was a 100-day meeting to discuss deficiencies in the PMA. FDA listed the current deficiencies in the application.
November 18, 2002	Q-MED	FDA	Letter	FDA stated PMA lacks information to complete review. This 10-page letter lists the deficiencies found by FDA.
December 27, 2002	FDA	Q-MED	Submission	Provided a complete response to FDA’s November 18, 2002 letter. Some

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Date	To	From	Type	Summary
				additional information was included as well to update the PMA. Also, provided comments regarding the need for a Panel meeting.
May 5, 2003	Q-MED	FDA	Letter	Received a deficiency letter from FDA.
June 16, 2003	FDA	Q-MED	Submission	Provided a complete response to the FDA deficiency letter of May 5, 2003. Provided data for risk assessment for residual BDDE, adverse events for other countries, safety data on specific ethnic groups.
Aug 8, 2003	FDA	Q-MED	Letter	Notified FDA that the letter represents the final report for the IDE and stated that the final report was submitted in the PMA. No further clinical trials are anticipated.
November 21, 2003				Advisory Panel meeting
December 12, 2003	Q-MED	FDA	Approval Letter	FDA approved the PMA for mid-to-deep dermal implantation for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds. There was agreement to perform a Phase IV study.

**PLEASE NOTE:** IDE G990258 was submitted by Q-MED Scandanavia on October 14, 1999 and became effective on August 4, 2000. P020023 was submitted by Q-MED Scandinavia, Inc. on June 19, 2002, and approved by the FDA on December 12, 2003. Q-MED Scandinavia, Inc. is a wholly owned subsidiary of Q-MED AB. An authorization from Q-MED Scandinavia, Inc. to Q-MED AB, to rely upon the activities of Q-MED Scandinavia, Inc. before the FDA during the regulatory review period in making its applications for extension and extension of patent term, and granting the Commissioner for Patents and the Secretary for Health and Human Services and/or Commissioner of Food and Drugs the right to refer to IDE G990258 and P020023 in determining the eligibility of Q-MED AB for such extensions, is attached as ATTACHMENT G.

**(12) ELIGIBILITY FOR EXTENSION OF PATENT TERM**

In the opinion of Q-MED AB, U.S. Patent No. 5,827,937 is eligible for the requested extension of patent term, and the length of extension claimed is **879 days**.

The length of extension of the term of U.S. Patent No. 5,827,937 of **879 days** is based upon 37 C.F.R. §1.777, which states that the term of the patent for a medical device will be extended by the length of the regulatory review period for the product as determined by the Secretary of Health and Human Services, reduced as appropriate pursuant to paragraphs (d)(1) through (d)(6) of this section.

**37 C.F.R. §1.777(c)**

First of all, the length of the regulatory review period for a medical device will be determined by the Secretary of Health and Human Services. Under 35 U.S.C. 156(g)(3)(B), it is the sum of:

(1) The number of days in the period beginning on the date a clinical investigation on humans involving the device was begun and ending on the date an application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act; and

(2) The number of days in the period beginning on the date the application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act, and ending on the date such application was approved

under such Act or the period beginning on the date a notice of completion of a product development protocol was initially submitted under section 515(f)(5) of the Act and ending on the date the protocol was declared completed under section 515(f)(6) of the Act.

37 C.F.R. §1.777(c)(1)

With respect to 37 C.F.R. §1.777(c)(1), the date a clinical investigation on humans involving the device was begun was **December 28, 1999**. The date an application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act was **June 19, 2002**.

Thus, the “number of days in the period beginning on the date a clinical investigation on humans involving the device was begun and ending on the date an application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act” is the number of days between **December 28, 1999** and **June 19, 2002**, which is **904 days**.

37 C.F.R. §1.777(c)(2)

With respect to 37 C.F.R. §1.777(c)(2), the date the application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act was **June 19, 2002**. The date such application was approved under such Act was **December 12, 2003**.

Thus, the number of days in “the period beginning on the date the application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act, and ending on the date such application was approved under such Act” is the number of days between **June 19, 2002** and **December 12, 2003**, which is **541 days**.

Thus, the sum of the periods in 37 C.F.R. §1.777(c)(1) and 37 C.F.R. §1.777(c)(2) is equal to 904+541, which is **1445 days**.

**37 C.F.R. §1.777(d)**

Next, the regulatory review period for the product, as determined by the Secretary of Health and Human Services, is reduced as appropriate pursuant to paragraphs (d)(1) through (d)(6) of 37 C.F.R. §1.777(d). At the outset, we note that 37 C.F.R. §1.777(d)(6) is **not applicable**, since U.S. Patent No. 5,827,937 was **not** “issued before September 24, 1984.”

37 C.F.R. §§1.777(d)(1)-(5) state that:

The term of the patent as extended for a medical device will be determined by --

(1) Subtracting from the number of days determined by the Secretary of Health and Human Services to be in the regulatory review period pursuant to paragraph (c) of this section:

(i) The number of days in the periods of paragraphs (c)(1) and (c)(2) of this section which were on and before the date on which the patent issued;

(ii) The number of days in the periods of paragraphs (c)(1) and (c)(2) of this section during which it is determined under 35 U.S.C. 156(d)(2)(B) by the Secretary of Health and Human Services that applicant did not act with due diligence;

(iii) One-half the number of days remaining in the period defined by paragraph (c)(1) of this section after that period is reduced in accordance with paragraphs (d)(1)(i) and (ii) of this section; half days will be ignored for purposes of subtraction;

(2) By adding the number of days determined in paragraph (d)(1) of this section to the original term of the patent as shortened by any terminal disclaimer;

(3) By adding 14 years to the date of approval of the application under section 515 of the Federal Food, Drug, and Cosmetic Act or the date a product development protocol was declared completed under section 515(f)(6) of the Act;

(4) By comparing the dates for the ends of the periods obtained pursuant to paragraphs (d)(2) and (d)(3) of this section with each other and selecting the earlier date;

(5) If the original patent was issued after September 24, 1984,

(i) By adding 5 years to the original expiration date of the patent or earlier date set by terminal disclaimer; and

(ii) By comparing the dates obtained pursuant to paragraphs (d)(4) and (d)(5)(i) of this section with each other and selecting the earlier date;

37 C.F.R. §1.777(d)(1)

The periods in paragraph d(1) are calculated as follows:

(i) The number of days in the periods of paragraphs (c)(1) and (c)(2) of this section which were on and before the date on which the patent issued would be **zero**.

(In this regard, the patent issued on **October 27, 1998**. The clinical investigation on humans involving the device did not begin until **December 28, 1999** and the application under section 515 of the Federal Food, Drug, and Cosmetic Act was not submitted until **June 19, 2002**.)

(ii) In the Applicant's opinion, marketing applicant acted with due diligence as defined at 35 U.S.C. §156(d)(3) during the above calculated periods of paragraphs (c) (1) and (c)(2). Thus, **zero days** are subtracted from the regulatory review period.

(iii) As mentioned above, the number of days calculated according to paragraphs (d)(1)(i) and (ii) of this section are both zero. Thus, “one-half the number of days remaining in the period defined by paragraph (c)(1) after that period is reduced in accordance with paragraphs (d)(1)(i) and (ii) of this section” would be  $=(904-0)/2$ , or **452 days**.

Thus, subtracting from the number of days determined by the Secretary of Health and Human Services to be in the regulatory review period pursuant to paragraph (c) of this section would result in 1445-452 days, which is **993 days**.

37 C.F.R. §1.777(d)(2)

The number of days determined in paragraph (d)(1) of this section would be **993 days**, as described in detail above.

The original term of the patent as shortened by any terminal disclaimer would be 20 years from issue, *i.e.*, **July 17, 2015**.

Thus, adding the number of days determined in paragraph (d)(1) of this section to the original term of the patent as shortened by any terminal disclaimer would be:

= 993 days + July 17, 2015

= **April 5, 2018**

37 C.F.R. §1.777(d)(3)

The date of approval of the application under section 515 of the Federal Food, Drug, and Cosmetic Act was December 12, 2003.

Thus, adding 14 years to the date of approval of the application under section 515 of the Federal Food, Drug, and Cosmetic Act would be:

= December 12, 2003 + 14 years

= **December 12, 2017.**

37 C.F.R. §1.777(d)(4)

The dates for the ends of the periods obtained pursuant to paragraphs (d)(2) and (d)(3) of this section are **April 5, 2018** and **December 12, 2017** respectively.

Of these two dates, the earlier date is **December 12, 2017.**

37 C.F.R. §1.777(d)(5)

(i) The original expiration date of the patent would be July 17, 2015. Adding 5 years to the original expiration date of the patent or earlier date set by terminal disclaimer would result in a date of July 17, 2015 + 5 years, *i.e.*, **July 17, 2020.**

(ii) The dates obtained pursuant to paragraphs (d)(4) and (d)(5)(i) of this section are  
**December 12, 2017** and **July 17, 2020** respectively.

Of these two dates, the earlier date is **December 12, 2017**.

**(13) DUTY OF DISCLOSURE**

Q-MED AB acknowledges a duty to disclose to the Director of the U.S. Patent & Trademark Office and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought herein.

Application For Extension Of  
Patent Term Under 35 U.S.C. § 156  
for U.S. Patent No. 5,827,937  
Attorney Docket No.: 003300-356

**(14) FEES**

The Director is hereby authorized to charge the amount of \$ 1,120 (37 C.F.R. § 1.20(j)(1)) to Deposit Account No. 02-4800 for receiving and acting upon the application for extension.

The Director is hereby also authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Application For Extension Of  
Patent Term Under 35 U.S.C. § 156  
for U.S. Patent No. 5,827,937  
Attorney Docket No.: 003300-356

**(15) NAME AND ADDRESS FOR CORRESPONDENCE**

Please address all inquiries and correspondence relating to this application for patent extension to:

Benton S. Duffett  
BURNS, DOANE, SWECKER & MATHIS, L.L.P.  
P.O. Box 1404  
Alexandria, Virginia 22313-1404  
Telephone: (703) 836-6620  
Facsimile: (703) 836-2021

**(16) MULTIPLE COPIES**

This application for extension, together with the appended ATTACHMENTS A through H, is being submitted in original form along with three copies. The undersigned hereby certifies that the copies of this application for extension, together with the appended ATTACHMENTS A through H, filed herewith are true and correct copies.

**(17) DECLARATION**

I, Benton S. Duffett (the undersigned duly authorized agent for Q-MED AB) do hereby declare as follows:

(a) I am a patent attorney authorized to practice before the U.S. Patent & Trademark Office and am authorized to represent Q-MED AB in this application for patent term extension by virtue of a Power of Attorney executed on August 19, 1997 (a copy of the Power of Attorney is attached hereto as ATTACHMENT H);

(b) I have reviewed and understand the contents of this application for patent term extension;

(c) I believe that U.S. Patent No. 5,827,937 is subject to patent term extension pursuant to 35 U.S.C. § 156 and 37 C.F.R. §§ 1.710, 720, 740 and 777;

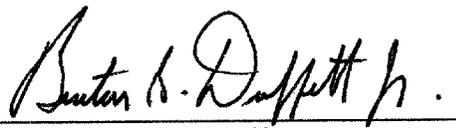
(d) I believe that an extension of the length claimed is justified under 35 U.S.C. § 156 and the applicable regulations; and

(e) I believe that U.S. Patent No. 5,827,937 meets the conditions for extension of the term of a patent set forth in 37 C.F.R. § 1.720.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application being submitted herewith or any extension of patent term granted thereon.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By:   
Benton S. Duffett, Jr.  
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Date: February 10, 2004