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[54] **BIODEGRADABLE IN-SITU FORMING IMPLANTS AND METHODS OF PRODUCING THE SAME**

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[*] Notice: The term of this patent shall not extend beyond the expiration date of Pat. No. 4,938,763.

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Related U.S. Application Data

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[52] **U.S. Cl.** **523/113**; 523/115; 604/51; 604/54; 604/56; 604/290; 525/408; 525/412; 525/413; 525/937; 424/422; 424/78.38; 524/96; 524/601

[58] **Field of Search** 523/113, 115; 524/96, 601; 525/937, 408, 412, 413; 424/422, 78.38; 604/51, 54, 26, 290

[56] **References Cited**

U.S. PATENT DOCUMENTS

2,155,658	4/1939	Herrmann	514/772.2
3,068,188	12/1962	Beste	524/173
3,218,283	11/1965	Miller	524/173
3,219,527	11/1965	Gurney	424/435
3,328,246	6/1967	Gottfried	424/435
3,463,158	8/1969	Schmitt .	
3,520,949	7/1970	Shepherd	128/156
3,696,811	10/1972	Chen	126/156
3,755,558	8/1973	Scribner .	
3,760,034	9/1973	Critchfield	525/411
3,767,784	10/1973	Glick	128/156
3,887,699	6/1975	Yolles	424/477
3,931,678	1/1976	O'Sullivan	433/228.1
3,935,308	1/1976	Wise .	
3,939,111	2/1976	Schollenberger	524/233
4,148,871	4/1979	Pitt	424/426
4,161,948	7/1979	Bichon	128/156
4,408,023	10/1983	Gould	528/75
4,439,420	3/1984	Mattei et al.	424/78.38
4,443,430	4/1984	Mattei et al.	424/78.38
4,447,562	5/1984	Ivani	523/105
4,450,150	5/1984	Sidman	424/426
4,491,479	1/1985	Lauchenauer	128/156
4,568,536	2/1986	Kronenthal	514/900
4,570,629	2/1986	Widra	128/156
4,582,640	4/1986	Smestad	128/DIG. 8
4,595,713	6/1986	St. John	523/109
4,631,188	12/1986	Stoy	424/81
4,650,665	3/1987	Kronenthal	424/435
4,663,077	5/1987	Rei .	
4,677,139	6/1987	Feinmann	128/90
4,702,917	10/1987	Schindler	424/422
4,715,369	12/1987	Suzuki	424/435
4,745,160	5/1988	Churchill	523/105
4,767,627	8/1988	Caldwell	424/426
4,767,861	8/1988	Boulware	424/422
4,772,470	9/1988	Inoue	424/435
4,774,227	9/1988	Piez	128/DIG. 8
4,780,320	10/1988	Baker	424/486

(List continued on next page.)

FOREIGN PATENT DOCUMENTS

1261549	9/1989	Canada .	
0140766	5/1985	European Pat. Off.	424/435
0159293	10/1985	European Pat. Off. .	
169016	1/1986	European Pat. Off. .	
0241178	10/1987	European Pat. Off. .	
0244118	11/1987	European Pat. Off. .	
0537559 A1	4/1993	European Pat. Off. .	
0539751 A1	5/1993	European Pat. Off. .	
0560014 A1	9/1993	European Pat. Off. .	
0649662 A1	4/1995	European Pat. Off. .	
2126270	10/1972	France .	
29 17 037	4/1980	Germany	433/228.1
WO 85/00969	3/1985	WIPO .	
WO 85/02092	5/1985	WIPO .	

OTHER PUBLICATIONS

Encyclopedia of Polymer Science and Engineering, vol. 2, pp. 236–237 (Biodegradable Polymers), John Wiley & Sons, Inc. (1985).

Billmeyer, Textbook of Polymer Science (Third Edition), pp. 390–391, John Wiley & Son, New York (1984).

Gilding, Biodegradable Polymers (Chapter 9), pp. 210–232, Biocompatibility of Clinical Implant Materials, (1976).

Hawley's Condensed Chemical Dictionary (11th Ed.) pp. 224, 555 and 567, Van Nostrand Reinhold Co., N.Y., N.Y., (1987).

Holland, Polymers for Biodegradable Medical Devices, 1. The Potential of Polyesters and Controlled Macromolecular Release Systems, J. of Controlled Release 4: 155–180 (1986).

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[57] **ABSTRACT**

A biodegradable polymer is provided for use in providing syringeable, in-situ forming, solid biodegradable implants for animals. The polymer is placed into the animal in liquid form and cures to form the implant in-situ. A thermoplastic system to form said implant comprises the steps of dissolving a non-reactive polymer in biocompatible solvent to form a liquid, placing the liquid within the animal, and allowing the solvent to dissipate to produce the implant. An alternative, thermosetting system comprises mixing together effective amounts of a liquid acrylic ester terminated, biodegradable prepolymer and a curing agent, placing the liquid mixture within an animal and allowing the prepolymer to cure to form the implant. Both systems provide a syringeable, solid biodegradable delivery system by the addition of an effective level of biologically active agent to the liquid before injection into the body.

43 Claims, 2 Drawing Sheets