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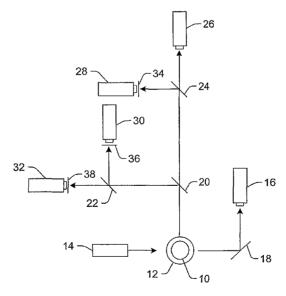
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS FOR ALTERING SURFACE CHARACTERISTICS OF MICROSPHERES



(57) Abstract: Various methods for forming dyed microspheres are provided. One method includes activating a chemical structure coupled to a dye using heat or light to form a reaction intermediate in the presence of a microsphere. The reaction intermediate covalently attaches to a polymer of the microsphere thereby coupling the dye to the polymer and forming the dyed microsphere. Additional methods are provided for forming a dyed microsphere coupled to a molecule. These methods include dyeing the microspheres as described above in addition to synthesizing the molecule on an outer surface of the dyed microspheres. A population of dyed microspheres is also provided. Each of the dyed microspheres of the population includes a dye attached to a polymer of each of the dyed microspheres by a chemical structure. A coefficient of variation in dye characteristics of the population of dyed microspheres attributable to the dye is less than about 10%.



#### INTERNATIONAL SEARCH REPORT

International application No PCT/US2005/036264

A. CLASSIFICATION OF SUBJECT MATTER INV. G01N33/543 G01N33/546 G01N33/58 According to International Patent Classification (IPC) or to both national classification and IPC Minimum documentation searched (classification system followed by classification symbols) GO1N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, PAJ C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages Category\* 1 - 42US 2004/087032 A1 (CHANDLER MARK B ET AL) Χ 6 May 2004 (2004-05-06) the whole document In particular: paragraphs 2, 3, 11, 18-21, 28, 38, 41-51, 54-67 US 2003/028981 A1 (CHANDLER DON J ET AL) 13 February 2003 (2003-02-13) 1 - 42X the whole document In particular: paragraphs 1, 9-12, 21, 22, 30-40, 43, 49 and claims 1-40 -/--See patent family annex. X Further documents are listed in the continuation of Box C. Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search 15. 01. 2007 9 February 2006 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, ANGIONI, C

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# INTERNATIONAL SEARCH REPORT

International application No
PCT/US2005/036264

		PCT/US2005/036264					
C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT							
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.					
Х	WO 02/40698 A (SURROMED, INC) 23 May 2002 (2002-05-23) the whole document In particular: p. 1, l. 4-9; p. 6, l. 14-33; p. 10, l. 7-16; p. 13, l. 10 - p. 15, l. 15; p. 16, l. 21-33; p. 29, l. 11-24; p. 32, l. 1-14 and Figs. 1-6.	1-42					
X	US 5 763 203 A (UGELSTAD ET AL) 9 June 1998 (1998-06-09) the whole document In particular: col. 1, l. 4-7; col. 3, l. 1-46; col. 5, l. 50 - col. 6, l. 13; col. 10, l. 33 - col. 13, l. 32	1-42					
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International application No. PCT/US2005/036264

### INTERNATIONAL SEARCH REPORT

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Claims Nos.:  because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
A. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

# FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1 (in part),2,9-17 (in part),18,25-36 (in part)

A method for altering surface characteristics, a micro-sphere and kit comprising micro-spheres in which the micro-spheres are altered by coupling an enolic acid which contains at least one hydrophilic group.

2. claims: 1 (in part),3,9-17,19,25-36 (all in part)

A method for altering surface characteristics, a micro-sphere and kit comprising micro-spheres in which the micro-spheres are altered by coupling deltic acid.

3. claims: 1 (in part),3,9-17,19,25-36 (all in part)

A method for altering surface characteristics, a micro-sphere and kit comprising micro-spheres in which the micro-spheres are altered by coupling squaric acid.

4. claims: 1 (in part),3,9-17,19,25-36 (all in part)

A method for altering surface characteristics, a micro-sphere and kit comprising micro-spheres in which the micro-spheres are altered by coupling croconic acid.

5. claims: 1 (in part),3,9-17,19,25-36 (all in part)

A method for altering surface characteristics, a micro-sphere and kit comprising micro-spheres in which the micro-spheres are altered by coupling rhodizonic acid.

6. claims: 1 (in part),4,9-17 (in part),20,25-36 (in part)

A method for altering surface characteristics, a micro-sphere and kit comprising micro-spheres in which the micro-spheres are altered by coupling 5-substituted hydroxy tropolone.

7. claims: 1 (in part),5,9-17 (in part),21,25-36 (in part)

A method for altering surface characteristics, a micro-sphere and kit comprising micro-spheres in which the micro-spheres are altered by coupling cyanuric acid or cyanuric acid derivative.

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

8. claims: 1 (in part),6,9-17 (in part),22,25-36 (in part)

A method for altering surface characteristics, a micro-sphere and kit comprising micro-spheres in which the micro-spheres are altered by coupling dimethoxy triazine methylmorpholine modified to contain hyrophilic groups.

9. claims: 1 (in part),7,9-17 (in part),23,25-36 (in part)

A method for altering surface characteristics, a micro-sphere and kit comprising micro-spheres in which the micro-spheres are altered by coupling boronic acid or acid boronic acid derivative.

10. claims: 1 (in part),8,9-17 (in part),24,25-36 (in part)

A method for altering surface characteristics, a micro-sphere and kit comprising micro-spheres in which the micro-spheres are altered by coupling silicic acid or acid silicic acid derivative.

11. claims: 37-42 (in part)

A method for altering surface characteristics, a micro-sphere and kit comprising micro-spheres in which the micro-spheres are altered by coupling with an ionisable polar group in conjunction with a chemical group, wherein the chemical group is a sulfone group.

12. claims: 37-42 (in part)

A method for altering surface characteristics, a micro-sphere and kit comprising micro-spheres in which the micro-spheres are altered by coupling with an ionisable polar group in conjunction with a chemical group, wherein the chemical group is a carbonyl group.

## **INTERNATIONAL SEARCH REPORT**

International application No PCT/US2005/036264

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