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# United States Patent [19]

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May et al.

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[54] **CAPILLARY IMMUNOASSAY AND DEVICE THEREFOR COMPRISING MOBILIZABLE PARTICULATE LABELLED REAGENTS**

3,744,975 7/1973 Mailen ..... 23/259  
3,798,004 3/1974 Zerachia et al. .... 422/56

(List continued on next page.)

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### FOREIGN PATENT DOCUMENTS

6007486 7/1985 Australia .  
1185882 11/1981 Canada .

(List continued on next page.)

[73] Assignee: **Unilever Patent Holdings B.V.**, Netherlands

### OTHER PUBLICATIONS

[21] Appl. No.: **102,313**

Glad et al, Analytical Biochemistry (B5) 1978, pp. 180-187.  
Gribnau et al, J. Chromatography 376 (1986) pp. 175-189.

[22] Filed: **Jul. 15, 1993**

(List continued on next page.)

### Related U.S. Application Data

[60] Continuation of Ser. No. 876,449, Apr. 30, 1992, abandoned, which is a division of Ser. No. 795,266, Nov. 19, 1991, abandoned, which is a continuation of Ser. No. 294,146, filed as PCT/GB88/00322, Apr. 26, 1988, abandoned.

*Primary Examiner*—Carol A. Spiegel

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### Foreign Application Priority Data

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### ABSTRACT

[51] **Int. Cl.<sup>6</sup>** ..... **G01N 33/558**

[52] **U.S. Cl.** ..... **436/514; 422/56; 422/58; 422/60; 435/7.1; 435/962; 435/970; 435/971; 435/973; 436/510; 436/518; 436/541; 436/805; 436/810; 436/817; 436/818**

[58] **Field of Search** ..... **722/56-58; 436/501, 436/530, 810, 814, 514, 515, 518, 523, 524, 541, 510, 538, 817, 818; 435/810, 7.92-7.95, 970; 422/60; 427/2, 2.11**

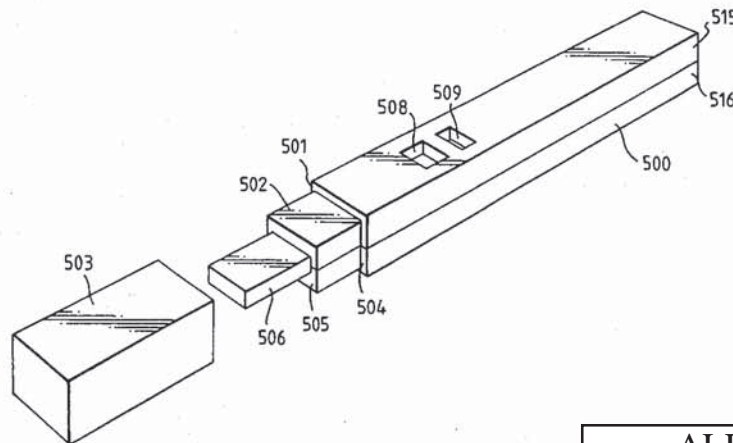
An analytical test device useful for example in pregnancy testing, includes a hollow casing (500) constructed of moisture-impervious solid material, such as plastics materials, containing a dry porous carrier (510) which communicates indirectly with the exterior of the casing via a bibulous sample receiving member (506) which protrudes from the casing such that a liquid test sample can be applied to the receiving member and permeate therefrom to the porous carrier, the carrier containing in a first zone a labelled specific binding reagent is freely mobile within the porous carrier when in the moist state, and in a second zone spatially distinct from the first zone unlabelled specific binding reagent for the same analyte which unlabelled reagent is permanently immobilised on the carrier material and is therefore not mobile in the moist state, the two zones being arranged such that liquid sample applied to the porous carrier can permeate via the first zone into the second zone, and the device incorporating an aperture (508) in the casing, enabling the extent (if any) to which the labelled reagent becomes bound in the second zone to be observed. Preferably the device includes a removable cap for the protruding bibulous member.

### References Cited

#### U.S. PATENT DOCUMENTS

Re. 29,169 4/1977 Schuurs et al. .... 435/7.8  
3,410,839 11/1968 De Carvalho .  
3,420,205 1/1969 Morison ..... 435/805 X  
3,437,449 4/1969 Luckey ..... 23/254  
3,475,129 10/1969 Peurifoy et al. .... 23/230  
3,620,677 11/1971 Morison ..... 422/56  
3,666,421 5/1972 Price .  
3,720,760 3/1973 Bennich et al. .... 424/1  
3,723,064 3/1973 Liotta ..... 23/230 R

**36 Claims, 5 Drawing Sheets**



ALERE EX 1011

## U.S. PATENT DOCUMENTS

|           |         |                          |           |           |         |                   |           |
|-----------|---------|--------------------------|-----------|-----------|---------|-------------------|-----------|
| 3,811,840 | 5/1974  | Bauer et al.             | 422/56    | 4,469,787 | 9/1984  | Woods             | 435/7.4   |
| 3,850,578 | 11/1974 | McConnell                | 436/536   | 4,474,878 | 10/1984 | Halbert et al.    | 435/5     |
| 3,876,504 | 4/1975  | Koffler                  |           | 4,483,921 | 11/1984 | Cole              | 435/7.9   |
| 3,915,647 | 10/1975 | Wright                   |           | 4,483,928 | 11/1984 | Suzuta et al.     | 436/519   |
| 3,954,564 | 5/1976  | Mennen                   | 435/805 X | 4,483,929 | 11/1984 | Szoka             | 436/533   |
| 3,981,981 | 9/1976  | Reunanen                 | 436/535   | 4,486,530 | 12/1984 | David et al.      | 435/7.9   |
| 4,016,043 | 4/1977  | Schuurs et al.           | 435/5     | 4,493,793 | 1/1985  | Chu               |           |
| 4,018,662 | 4/1977  | Ruhenstroth-Bauer et al. | 204/299 R | 4,503,143 | 3/1985  | Gerber et al.     | 435/7.36  |
| 4,022,876 | 5/1977  | Anbar                    | 424/1     | 4,515,889 | 5/1985  | Klose et al.      | 435/4     |
| 4,042,335 | 8/1977  | Clement                  | 422/56    | 4,517,288 | 5/1985  | Giegel et al.     | 435/5     |
| 4,087,326 | 5/1978  | Kereluk                  | 435/31    | 4,518,565 | 5/1985  | Boger et al.      | 435/805   |
| 4,087,332 | 5/1978  | Hansen                   | 435/33    | 4,526,871 | 7/1985  | Avrameas et al.   | 435/7.25  |
| 4,094,647 | 6/1978  | Deutsch et al.           | 435/4     | 4,552,839 | 11/1985 | Gould             |           |
| 4,116,638 | 9/1978  | Kenoff                   | 422/99    | 4,554,256 | 11/1985 | Sasser et al.     | 436/510   |
| 4,120,945 | 10/1978 | Gutcho et al.            | 436/531   | 4,568,102 | 2/1986  | Nugatomo et al.   | 435/805   |
| 4,122,030 | 10/1978 | Smith et al.             | 252/313   | 4,587,102 | 5/1986  | Nagatomo et al.   | 422/56    |
| 4,123,173 | 10/1978 | Bullock et al.           | 356/246   | 4,590,170 | 5/1986  | Akiyoshi et al.   | 436/533   |
| 4,133,639 | 1/1979  | Harte                    | 436/518   | 4,592,338 | 6/1986  | Blackmore         | 128/897   |
| 4,145,186 | 3/1979  | Andersen                 | 436/1     | 4,594,327 | 6/1986  | Zuk               |           |
| 4,166,102 | 8/1979  | Johnson                  | 436/530   | 4,595,656 | 6/1986  | Allen et al.      | 435/7.9   |
| 4,166,105 | 8/1979  | Hirschfeld               | 424/8     | 4,608,246 | 8/1986  | Bayer et al.      | 424/11    |
| 4,168,146 | 9/1979  | Grubb et al.             | 435/7.92  | 4,650,769 | 3/1987  | Kakimi et al.     | 436/533   |
| 4,169,138 | 9/1979  | Jonsson                  | 436/524   | 4,656,129 | 4/1987  | Wagner            | 435/7.1   |
| 4,180,383 | 12/1979 | Johnson                  | 422/69    | 4,659,678 | 4/1987  | Forrest et al.    | 436/512   |
| 4,191,533 | 3/1980  | Bohn et al.              | 436/515   | 4,666,866 | 5/1987  | Krauth            | 436/518   |
| 4,219,335 | 8/1980  | Ebersole                 | 436/525   | 4,668,638 | 5/1987  | Janoff et al.     | 436/506   |
| 4,225,558 | 9/1980  | Peterson et al.          | 422/72    | 4,670,406 | 6/1987  | Allen et al.      | 436/500   |
| 4,230,683 | 10/1980 | Decker                   | 436/518   | 4,678,757 | 7/1987  | Rapkin            |           |
| 4,233,029 | 11/1980 | Columbus                 | 436/174   | 4,690,907 | 9/1987  | Hibino            | 436/514   |
| 4,233,286 | 11/1980 | Soothill et al.          | 436/507   | 4,693,970 | 9/1987  | O'Connell et al.  | 435/7.91  |
| 4,237,234 | 12/1980 | Meunier                  | 435/301   | 4,695,554 | 9/1987  | O'Connell         |           |
| 4,244,916 | 1/1981  | Guigan                   | 422/72    | 4,703,017 | 10/1987 | Campbell et al.   | 436/501   |
| 4,244,940 | 1/1981  | Jeong et al.             | 436/500   | 4,707,450 | 11/1987 | Nason             | 435/805 X |
| 4,246,339 | 1/1981  | Cole et al.              | 435/5     | 4,713,249 | 12/1987 | Schruder          | 424/1.37  |
| 4,248,965 | 2/1981  | Mochida et al.           | 435/7.92  | 4,725,406 | 2/1988  | Compton et al.    | 422/58    |
| 4,256,725 | 3/1981  | Rutner et al.            | 436/518   | 4,740,468 | 4/1988  | Weng et al.       | 435/7.91  |
| 4,258,001 | 3/1981  | Pierce et al.            | 422/56    | 4,742,011 | 5/1988  | Blake et al.      | 436/518   |
| 4,267,270 | 5/1981  | Stout                    | 435/7.93  | 4,743,560 | 5/1988  | Campbell et al.   | 436/501   |
| 4,270,921 | 6/1981  | Graas                    | 436/67    | 4,757,002 | 7/1988  | Joo               | 435/7.92  |
| 4,274,832 | 6/1981  | Wu et al.                | 435/11    | 4,775,515 | 10/1988 | Cottingham        | 422/101   |
| 4,278,651 | 7/1981  | Hales                    | 436/532   | 4,803,170 | 2/1989  | Stanton et al.    | 422/61    |
| 4,279,862 | 7/1981  | Bretaudiere et al.       | 422/72    | 4,806,311 | 2/1989  | Greenquist        | 435/7.4   |
| 4,279,885 | 7/1981  | Reese et al.             | 424/1.85  | 4,806,312 | 2/1989  | Greenquist        | 435/7.7   |
| 4,298,345 | 11/1981 | Sodickson et al.         | 422/56    | 4,810,470 | 3/1989  | Burkhardt         |           |
| 4,301,139 | 11/1981 | Feingers et al.          | 436/500   | 4,837,145 | 6/1989  | Liotta            |           |
| 4,302,536 | 11/1981 | Longenecker              | 435/7.25  | 4,837,168 | 6/1989  | de Jaenger et al. | 436/533   |
| 4,313,734 | 2/1982  | Leuvering                |           | 4,849,337 | 7/1989  | Calenoff et al.   | 435/7.92  |
| 4,315,908 | 2/1982  | Zer                      |           | 4,851,356 | 7/1989  | Canfield et al.   | 435/7.94  |
| 4,323,536 | 4/1982  | Columbus                 | 422/56    | 4,855,240 | 8/1989  | Rosenstein et al. | 436/514   |
| 4,326,008 | 4/1982  | Rembaum                  | 428/403   | 4,861,552 | 8/1989  | Masuda et al.     | 436/500   |
| 4,332,783 | 6/1982  | Pernice et al.           | 424/1     | 4,861,711 | 8/1989  | Friesen et al.    | 435/805   |
| 4,338,094 | 7/1982  | Elahi                    | 436/535   | 4,868,106 | 9/1989  | Ito et al.        | 435/805   |
| 4,347,312 | 8/1982  | Brown et al.             | 435/7.9   | 4,868,108 | 9/1989  | Baher et al.      | 435/7.82  |
| 4,363,874 | 12/1982 | Greenquist               | 435/7.7   | 4,874,710 | 10/1989 | Piran             | 436/518   |
| 4,366,241 | 12/1982 | Tom                      |           | 4,889,816 | 12/1989 | Davis             | 436/518   |
| 4,373,812 | 2/1983  | Stein et al.             | 356/246   | 4,900,663 | 2/1990  | Wie et al.        | 435/7.32  |
| 4,373,932 | 2/1983  | Gribanau et al.          | 436/501   | 4,904,583 | 2/1990  | Mapes et al.      | 435/7.92  |
| 4,374,925 | 2/1983  | Litman et al.            | 435/7.92  | 4,906,439 | 3/1990  | Grenner           |           |
| 4,380,580 | 4/1983  | Boguslaski et al.        | 435/5     | 4,916,056 | 4/1990  | Brown, III et al. | 435/7.92  |
| 4,411,518 | 10/1983 | Meserol et al.           | 356/39    | 4,938,927 | 7/1990  | Kelton et al.     | 422/64    |
| 4,425,438 | 1/1984  | Bauman et al.            | 436/527   | 4,954,452 | 9/1990  | Yost et al.       | 436/524   |
| 4,427,779 | 1/1984  | Reckel et al.            | 436/507   | 4,956,275 | 9/1990  | Zuk et al.        | 435/805   |
| 4,435,504 | 3/1984  | Zuk                      |           | 4,956,302 | 9/1990  | Gordon            |           |
| 4,442,204 | 4/1984  | Greenquist et al.        | 435/7.4   | 4,960,691 | 10/1990 | Gordon et al.     | 435/6     |
| 4,444,193 | 4/1984  | Fogt et al.              | 128/632   | 4,963,468 | 10/1990 | Olson             | 435/7.91  |
| 4,446,232 | 5/1984  | Liotta                   | 435/7.93  | 4,980,298 | 12/1990 | Blake et al.      | 436/518   |
| 4,447,526 | 5/1984  | Rupchock et al.          | 435/7.9   | 4,981,786 | 1/1991  | Dafforn et al.    | 435/805   |
| 4,452,901 | 6/1984  | Gordon                   |           | 5,026,653 | 6/1991  | Lee et al.        | 436/518   |
| 4,454,226 | 6/1984  | Ali et al.               | 435/7.21  | 5,030,558 | 7/1991  | Litman et al.     | 435/805   |
| 4,461,829 | 7/1984  | Greenquist               |           | 5,073,340 | 12/1991 | Covington         | 422/56    |
|           |         |                          |           | 5,073,484 | 12/1991 | Swanson           |           |
|           |         |                          |           | 5,089,394 | 2/1992  | Chun              |           |

|           |         |                     |          |
|-----------|---------|---------------------|----------|
| 5,120,643 | 6/1992  | Chang et al. ....   | 435/7.93 |
| 5,141,875 | 8/1992  | Keltron et al. .... | 436/514  |
| 5,354,692 | 10/1994 | Yang et al. ....    | 436/514  |

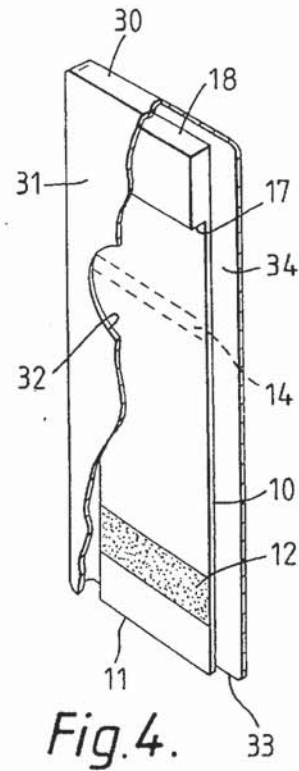
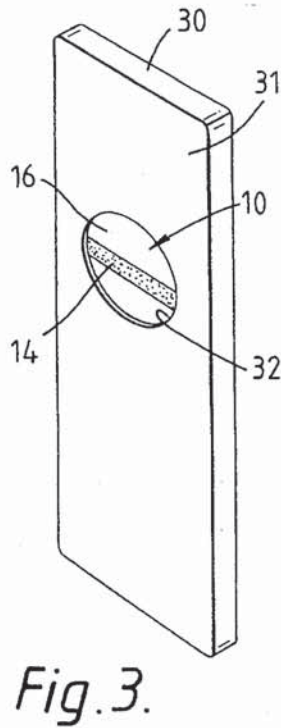
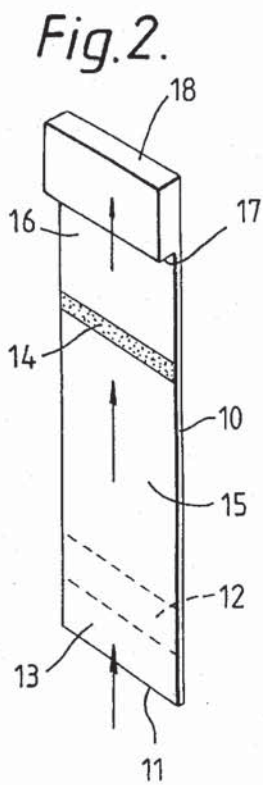
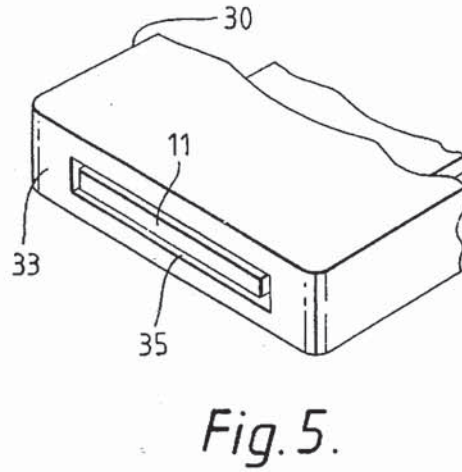
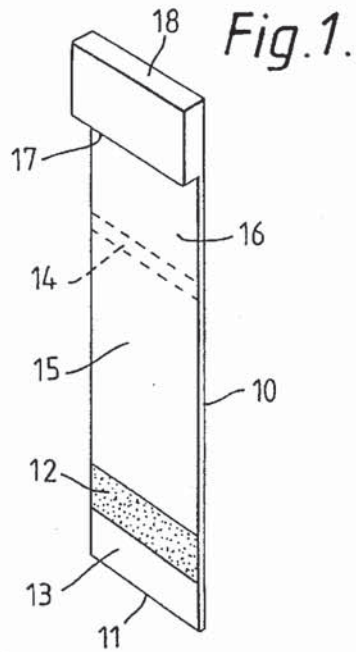
## FOREIGN PATENT DOCUMENTS

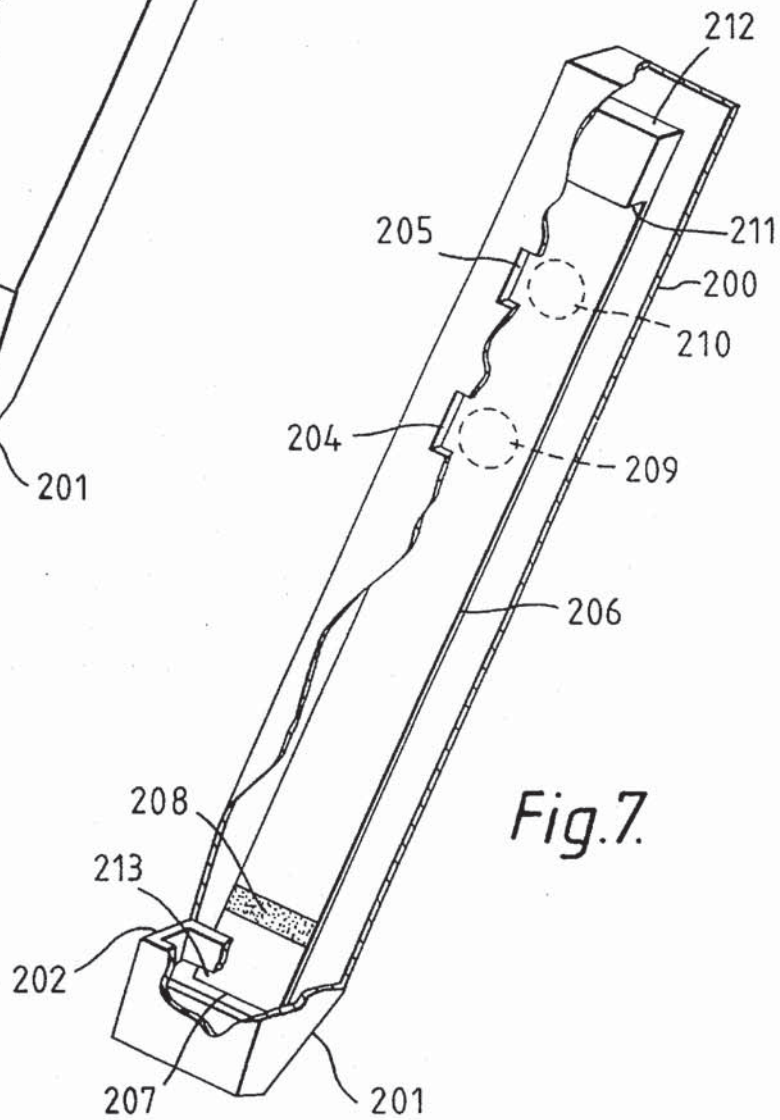
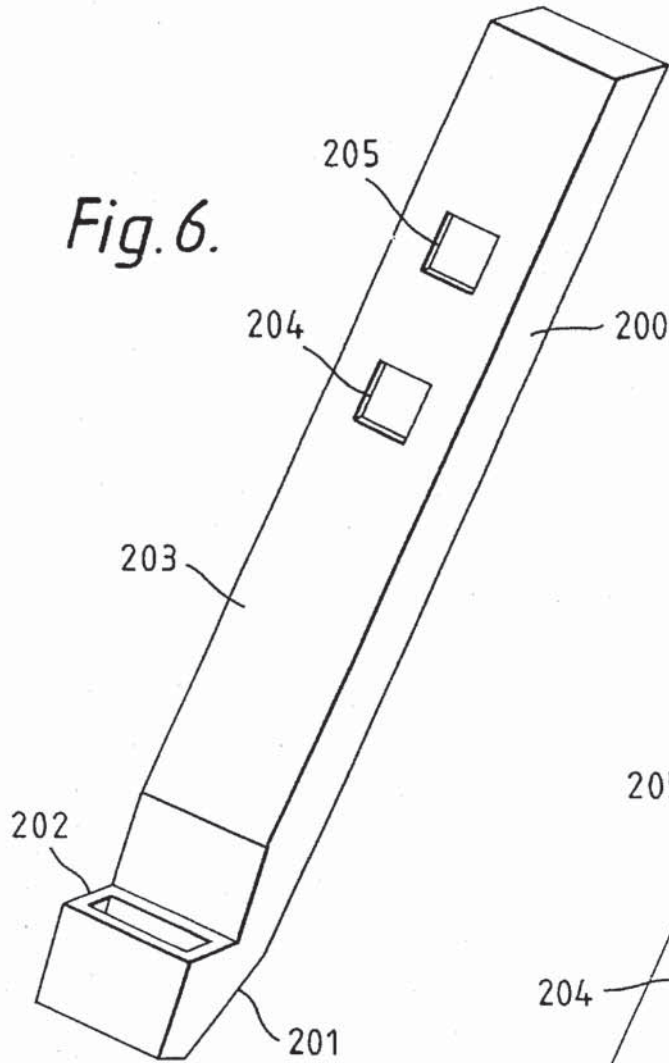
|            |         |                         |          |
|------------|---------|-------------------------|----------|
| 1185882    | 4/1985  | Canada .                |          |
| 1273306    | 8/1990  | Canada .                |          |
| 63810      | 11/1982 | European Pat. Off. .    |          |
| 97952      | 11/1984 | European Pat. Off. .    |          |
| 0125118    | 11/1984 | European Pat. Off. .    |          |
| 0149168    | 7/1985  | European Pat. Off. .    |          |
| 0212603    | 8/1985  | European Pat. Off. .    |          |
| 0154749    | 9/1985  | European Pat. Off. .    |          |
| 158746     | 10/1985 | European Pat. Off. .    |          |
| 0164180    | 12/1985 | European Pat. Off. .... | 435/7.9  |
| 0170746    | 2/1986  | European Pat. Off. .    |          |
| 10174247   | 3/1986  | European Pat. Off. .    |          |
| 30174247   | 3/1986  | European Pat. Off. .    |          |
| 0183442    | 6/1986  | European Pat. Off. .    |          |
| 0186100    | 7/1986  | European Pat. Off. .    |          |
| 0186799    | 7/1986  | European Pat. Off. .    |          |
| 0191640    | 8/1986  | European Pat. Off. .    |          |
| 0199205    | 10/1986 | European Pat. Off. .    |          |
| 0212599    | 3/1987  | European Pat. Off. .    |          |
| 0250137    | 12/1987 | European Pat. Off. .    |          |
| 0255342    | 2/1988  | European Pat. Off. .    |          |
| 0279097    | 8/1988  | European Pat. Off. .    |          |
| 0284232    | 9/1988  | European Pat. Off. .    |          |
| 0281201    | 9/1988  | European Pat. Off. .    |          |
| 0286371    | 10/1988 | European Pat. Off. .    |          |
| 0299428    | 1/1989  | European Pat. Off. .    |          |
| 0303784    | 2/1989  | European Pat. Off. .    |          |
| 48-5925    | 1/1973  | Japan .                 |          |
| 53-6465    | 2/1978  | Japan .                 |          |
| 59-122950  | 7/1984  | Japan .                 |          |
| 1502563    | 3/1978  | United Kingdom .....    | 435/7.9  |
| 1526708    | 9/1978  | United Kingdom .        |          |
| 2016687    | 9/1979  | United Kingdom .        |          |
| 2099578    | 1/1982  | United Kingdom .....    | 435/5    |
| 2086041    | 5/1982  | United Kingdom .        |          |
| 2111676    | 7/1983  | United Kingdom .        |          |
| WO80/01515 | 7/1980  | WIPO .                  |          |
| WO81/02790 | 10/1981 | WIPO .                  |          |
| WO85/01354 | 3/1985  | WIPO .....              | 435/7.34 |
| WO86/03839 | 7/1986  | WIPO .                  |          |
| WO86/04683 | 8/1986  | WIPO .                  |          |
| WO87/02774 | 5/1987  | WIPO .                  |          |

## OTHER PUBLICATIONS

- Leuversing et al, "Optimization of a Sandwich Sol Particle Immunoassay for Human Chorionic Gonadotrophin", *Journal of Immunological Methods*, Nov. 1, 1982, vol. 2, pp. 175-184.
- J. Sharon et al, "Detection of . . . Antibodies", *Proc. Nat. Acad. Sci. USA.*, 76, pp. 1420-1424, (1979).
- G.B. Wisdom, "Enzyme-Immunoassay", *Clinical Chemistry*, 22, 1248-1255, 1976.
- Micheel et al, "A Solid-Phase . . . Filters", *Acta Histochem*, vol. 71, pp. 15-18 (1982).
- Hawkes et al, "A Dot-Immunobinding Assay . . . Antibodies", *Analytical Biochemistry*, vol. 119, pp. 142-147 (1982).

- Esen et al, "A Simple and Rapid . . . Prolamins", *Analytical Biochemistry*, vol. 132, pp. 462-467 (1983).
- Bennett et al, "An improved Procedure . . . Supernatants", *Journal of Immunological Methods*, vol. 61, pp. 201-207 (1983).
- Norgaard-Pedersen, "A Highly Sensitive . . .  $\alpha$ -Fetoprotein", *Clin. Chem. Acta*, vol. 48, pp. 345-346, (1973).
- Syva/a Syntex Co., *AccuLevel TDM Assays*, Pamphlet, pp. 1-6, (1987).
- Laurell et al, "Electroimmunoassay", *Academic Press*, vol. 73, pp. 339, 340, 346-348 (1981).
- Gribnau et al, *The application of Colloidal dye particles . . . Immunoassay ("DIA")*, 1982, *Affinity Chromatography and related Techniques*, pp. 411-424.
- Kenna, et al., "Methods for Reducing Non-Specific Antibody Binding in Enzyme-Linked Immunosorbent Assays", *Journal of Immunological Methods*, 85 (1985) pp. 409-419.
- Vogt, Jr. et al., "Quantitative differences among various proteins as blocking agents for ELISA microtiter plates", *Journal of Immunological Methods*, 101 (1987) pp. 43-50.
- Romano et al., "An Antiglobulin Reagent Labelled With Colloidal Gold For Use In Electron Microscopy", *Immunochimistry*, 1974, vol. 11, pp. 521-522.
- Frens, G., *Nature Physical Science*, "Controlled Nucleation for the Regulation of the Particle Size in Monodisperse Gold Suspensions", vol. 241, Jan. 1, 1973, pp. 1-3.
- Hoye, Age, "Determination of Radiochemical . . . High-Voltage Electrophoresis", *Journal of Chromatography*, 28 (1967), pp. 379-384.
- Hsu, "Immunogold for Detection of Antigen on Nitrocellulose Paper", *Analytical Biochemistry*, vol. 142, (1984), pp. 221-225.
- Surek et al., "Visualization Of Antigenic . . . Method", *Biochemical and Biophysical Research Communications*, vol. 121, May 1, 1984, pp. 284-289.
- Geoghegan et al., "Passive Gold . . . Hemagglutination", *Journal of Immunological Methods*, 34, (1980), pp. 11-21.
- R. Brdicka, "Grundlagen Der Physikalischen Chemie", Berlin 1958, pp. 775, 784-787, (and English translation).
- Zsigmondy, "Ueber wassrige Losungen metallischen goldes", *Annalen der Chemie*, 301 (1898), pp. 28-55, (and English translation).
- Sahlbom, "Kolloidchemische Beihefte", Band II, (1910-1911), pp. 78-141, (and English translation).
- Zuk, et al. "Enzyme Immunochromatography - A Quantitative Immunoassay Requiring No Instrumentation", *Clinical Chemistry*, vol. 31, No. 7, 1985, pp. 1144-1150.
- Van Hell, et al., "Particle immunoassays", Chapter 4, *Alternative Immunoassays*, Collins, (1985) pp. 39-58.
- Bosch, M.G., "Enzym-und Sol Particle Immunoassays for Hormone.", *Archives of Gynecology and Obstetrics*, vol. 242, No. 1-4, (1987), pp. 509-512 (and English translation).
- Moecremans, et al., "Sensitive Visualization . . . Straining", *Journal of Immunological Methods*, 74 (1984) pp. 353-360.
- Leuversing, et al., "Sol Particle Immunoassay (SPIA)", *Abstract, Journal Of Immunoassay*, 1 (1), pp. 77-91 (1980).





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