



US005602040A

United States Patent [19]

[11] **Patent Number:** **5,602,040**

May et al.

[45] **Date of Patent:** ***Feb. 11, 1997**

[54] ASSAYS

[75] Inventors: **Keith May**, Bedfordshire; **Michael E. Prior**, Northamptonshire; **Ian Richards**, Bedford, all of England

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

[*] Notice: The term of this patent shall not extend beyond the expiration date of Pat. No. 5,599,721.

[21] Appl. No.: **241,675**

[22] Filed: **May 12, 1994**

Related U.S. Application Data

[60] Continuation of Ser. No. 876,448, 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.

[30] Foreign Application Priority Data

Apr. 27, 1987 [GB] England 8709873
Oct. 30, 1987 [GB] United Kingdom 8725457

[51] **Int. Cl.⁶** **G01N 33/558**

[52] **U.S. Cl.** **436/514; 436/501; 436/518; 436/523; 436/524; 436/525; 436/530; 436/541; 436/810; 436/814; 436/817; 436/818; 436/906; 435/962; 435/970; 435/975; 427/2.13; 422/60**

[58] **Field of Search** **422/56-58, 60; 436/501, 530, 514, 810, 814, 515, 518, 523, 524, 541, 817, 818, 906; 435/7.92-7.95, 970, 810, 962, 975; 427/2, 2.11, 2.13**

[56] References Cited

U.S. PATENT DOCUMENTS

3,410,839 11/1968 De Carvalho 422/58
3,420,205 1/1969 Morisson 116/114
3,620,677 11/1971 Morison 422/55

(List continued on next page.)

FOREIGN PATENT DOCUMENTS

1185882 4/1985 Canada 436/518
63810 11/1982 European Pat. Off. .
88636 9/1983 European Pat. Off. .

(List continued on next page.)

OTHER PUBLICATIONS

Glad et al, Analytical Biochemistry (B5) 1978, pp. 180-187.
Gribnau et al, J. Chromatography 376 (1986) pp. 175-189.
Kenna, et al., "Methods for Reducing Non-Specific Antibody Binding in Enzyme-Linked Immunosorbent Assays", Journal of Immunological Methods, 85 (1985) pp. 409-419.

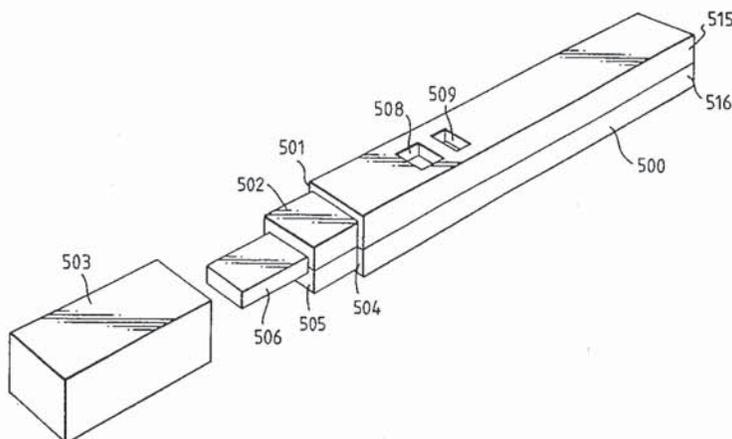
(List continued on next page.)

Primary Examiner—Carol A. Spiegel
Attorney, Agent, or Firm—Cushman Darby & Cushman, LLP

[57] ABSTRACT

An analytical test device useful for example in pregnancy testing, includes a hollow casing (500) constructed of moisture-imperious 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, wherein the mobility is facilitated by a material comprising sugar, in a amount effective to reduce interaction between the test strip and the labelled reagent, and in a second zone spatially distinct from the first zone unlabeled specific binding reagent for the same analyte which unlabelled reagent is permanently immobilized 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.

34 Claims, 5 Drawing Sheets



U.S. PATENT DOCUMENTS

3,666,421	5/1972	Price	422/56	158746	10/1985	European Pat. Off. .
3,811,840	5/1974	Bauer	422/56	0170746	2/1986	European Pat. Off. .
3,876,504	4/1975	Koffler	435/7.92	0186100	7/1986	European Pat. Off. .
3,915,647	10/1975	Wright	435/288.3	0186799	7/1986	European Pat. Off. .
3,954,564	5/1976	Mennen	435/37	0191640	8/1986	European Pat. Off. .
4,022,876	5/1977	Anbar	424/1	0199205	10/1986	European Pat. Off. .
4,042,335	8/1977	Clement	422/56	0212599	3/1987	European Pat. Off. .
4,094,647	6/1978	Deutsch et al.	435/4	0250137	12/1987	European Pat. Off. .
4,122,030	10/1978	Smith et al.	252/313 R	250137	12/1987	European Pat. Off. .
4,166,105	8/1979	Hirschfeld	424/8	0253581	1/1988	European Pat. Off. .
4,168,146	9/1979	Grubb et al.	435/7.92	0183442	6/1988	European Pat. Off. 436/518
4,169,138	9/1979	Jonsson	436/524	0279097	8/1988	European Pat. Off. .
4,235,601	11/1980	Deutsch et al.	422/56	0284232	9/1988	European Pat. Off. .
4,244,940	1/1981	Jeong et al.	424/1	0299428	1/1989	European Pat. Off. .
4,246,339	1/1981	Cole et al.	435/5	0303784	2/1989	European Pat. Off. .
4,302,536	11/1981	Longnecker	435/7.25	1526708	9/1978	United Kingdom .
4,313,734	2/1982	Leuvering	436/525	2016687	9/1979	United Kingdom .
4,315,908	9/1982	Zer	435/7.91	2086041	5/1982	United Kingdom .
4,366,241	12/1982	Tom et al.	435/7.91	2111676	7/1983	United Kingdom .
4,373,932	2/1983	Gribnau et al.	436/501	8102790	10/1981	WIPO 436/518
4,374,925	2/1983	Litman et al.	435/5	WO8603839	7/1986	WIPO .
4,435,504	3/1984	Zuk	435/7.91	WO86/04683	8/1986	WIPO .
4,452,901	5/1984	Gordon	435/7.92	WO87/02774	5/1987	WIPO .
4,461,829	7/1984	Greenquist	435/7.72			
4,493,793	1/1985	Chu	530/303			
4,518,565	5/1985	Boger et al.	422/58			
4,552,839	11/1985	Gould	455/7			
4,587,102	5/1986	Nugatomo et al.	422/56			
4,594,327	6/1986	Zuk	436/514			
4,608,246	8/1986	Bayer et al.	435/7.25			
4,659,678	4/1987	Forrest et al.	436/512			
4,678,757	7/1987	Rapkin	436/169			
4,695,554	9/1987	O'Connell	436/528			
4,703,017	10/1987	Campbell et al.	436/501			
4,707,450	11/1987	Nason	422/61			
4,725,406	2/1988	Compton et al.	422/58			
4,740,468	4/1988	Weng et al.	436/810			
4,742,011	5/1988	Blake et al.	436/518			
4,775,515	10/1988	Cottingham	422/58			
4,803,170	2/1989	Stanton et al.	422/56			
4,806,311	2/1989	Greenquist	422/58			
4,806,312	2/1989	Greenquist	422/58			
4,810,470	3/1989	Burkhardt	422/66			
4,837,145	6/1989	Liotta	435/7.94			
4,837,168	6/1989	de Jaeger et al.	436/533			
4,859,612	8/1989	Cole et al.	436/523			
4,861,552	8/1989	Mesuda et al.	436/530			
4,861,711	9/1989	Freese et al.	422/56			
4,868,106	9/1989	Ito et al.	436/530			
4,868,108	9/1989	Baher et al.	422/56			
4,906,439	3/1990	Grenner	422/56			
4,920,046	4/1990	McFarland et al.	435/7.9			
4,954,452	9/1990	Yost et al.	436/524			
4,956,275	9/1990	Zuk et al.	435/7.1			
4,956,302	9/1990	Gordon	436/161			
4,959,307	9/1990	Olson	435/7.9			
4,960,691	10/1990	Gordon	435/6			
4,981,786	1/1991	Duffurn et al.	422/56			
5,026,653	6/1991	Lee et al.	436/65			
5,030,558	7/1991	Witman et al.	436/810			
5,073,340	12/1991	Covington et al.	422/56			
5,073,484	12/1991	Swanson	435/7.92			
5,089,394	2/1992	Chun	435/34			
5,120,643	6/1992	Ching et al.	422/56			
5,141,850	8/1992	Cole et al.	436/525			

FOREIGN PATENT DOCUMENTS

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. .
0170746	2/1986	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. .
250137	12/1987	European Pat. Off. .
0253581	1/1988	European Pat. Off. .
0183442	6/1988	European Pat. Off. 436/518
0279097	8/1988	European Pat. Off. .
0284232	9/1988	European Pat. Off. .
0299428	1/1989	European Pat. Off. .
0303784	2/1989	European Pat. Off. .
1526708	9/1978	United Kingdom .
2016687	9/1979	United Kingdom .
2086041	5/1982	United Kingdom .
2111676	7/1983	United Kingdom .
8102790	10/1981	WIPO 436/518
WO8603839	7/1986	WIPO .
WO86/04683	8/1986	WIPO .
WO87/02774	5/1987	WIPO .

OTHER PUBLICATIONS

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", *Immunochemistry*, 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).

Mocremans, et al., "Sensitive Visualization . . . Straining", *Journal of Immunological Methods*, 74 (1984) pp. 353-360.

Leuvering, et al., "Sol Particle Immunoassay (SPIA)", *Abstract, Journal of Immunoassay*, 1(1), pp. 77-91 (1980).

Leuvering 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.

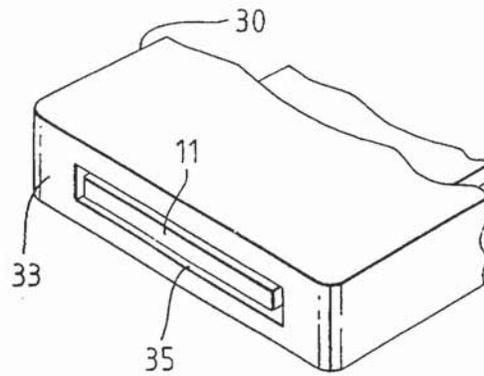
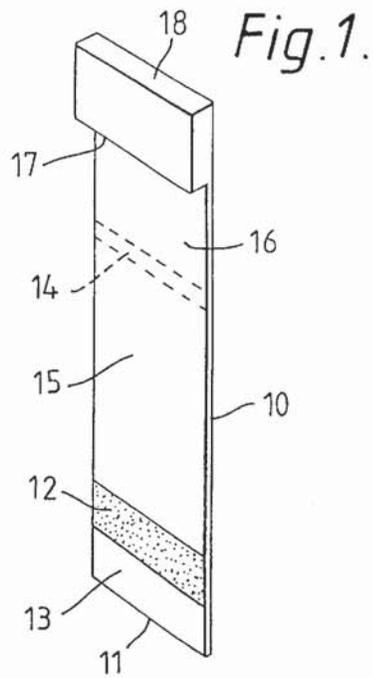


Fig. 5.

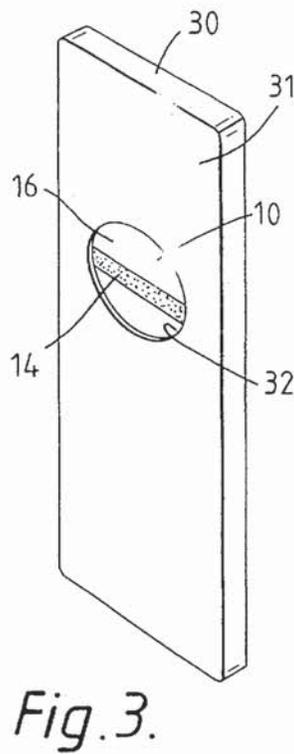
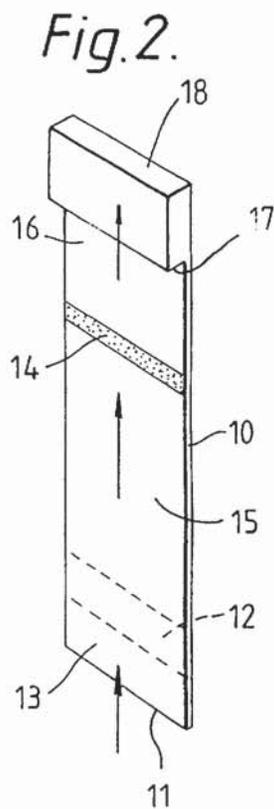


Fig. 3.

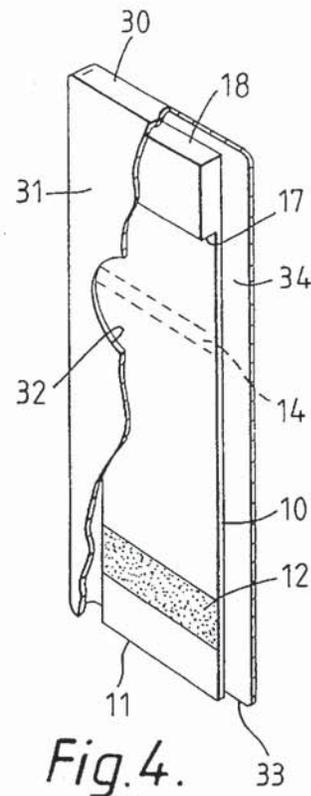
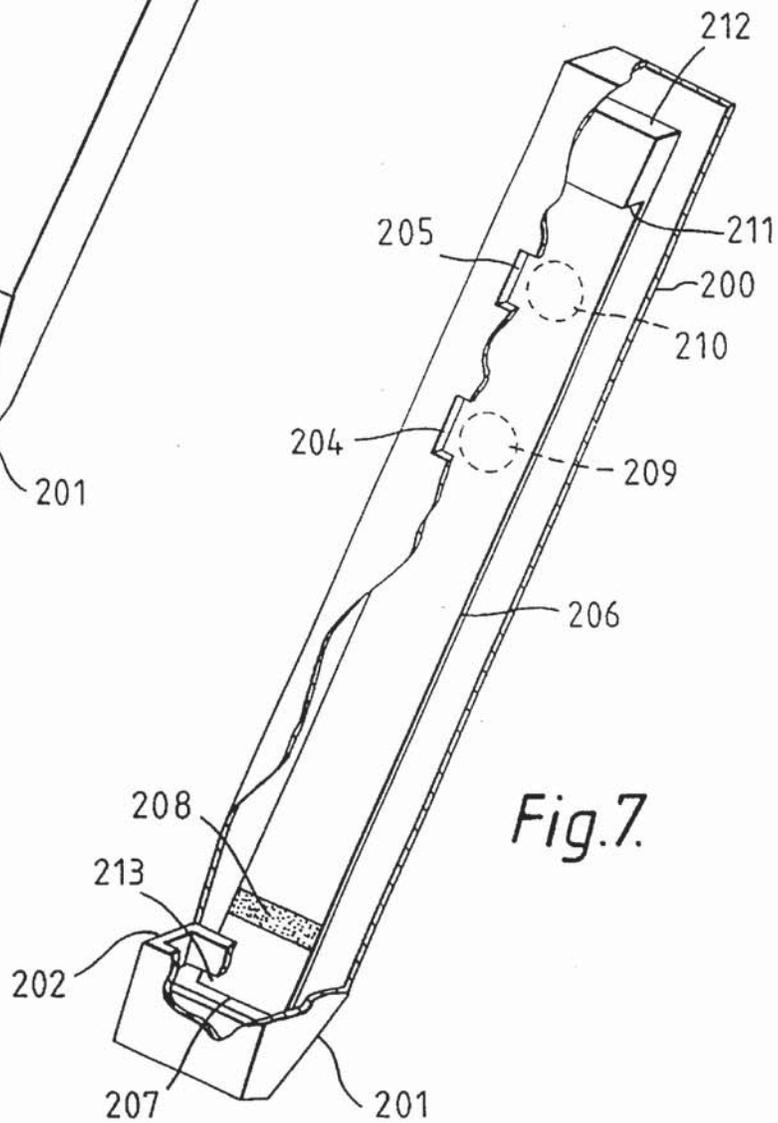
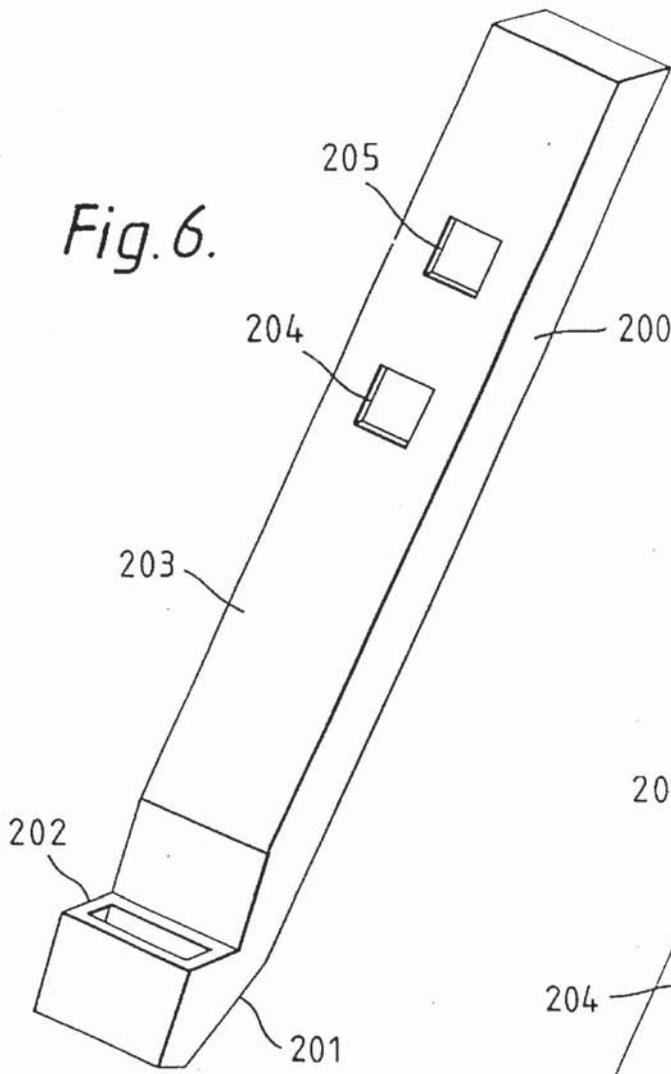


Fig. 4.



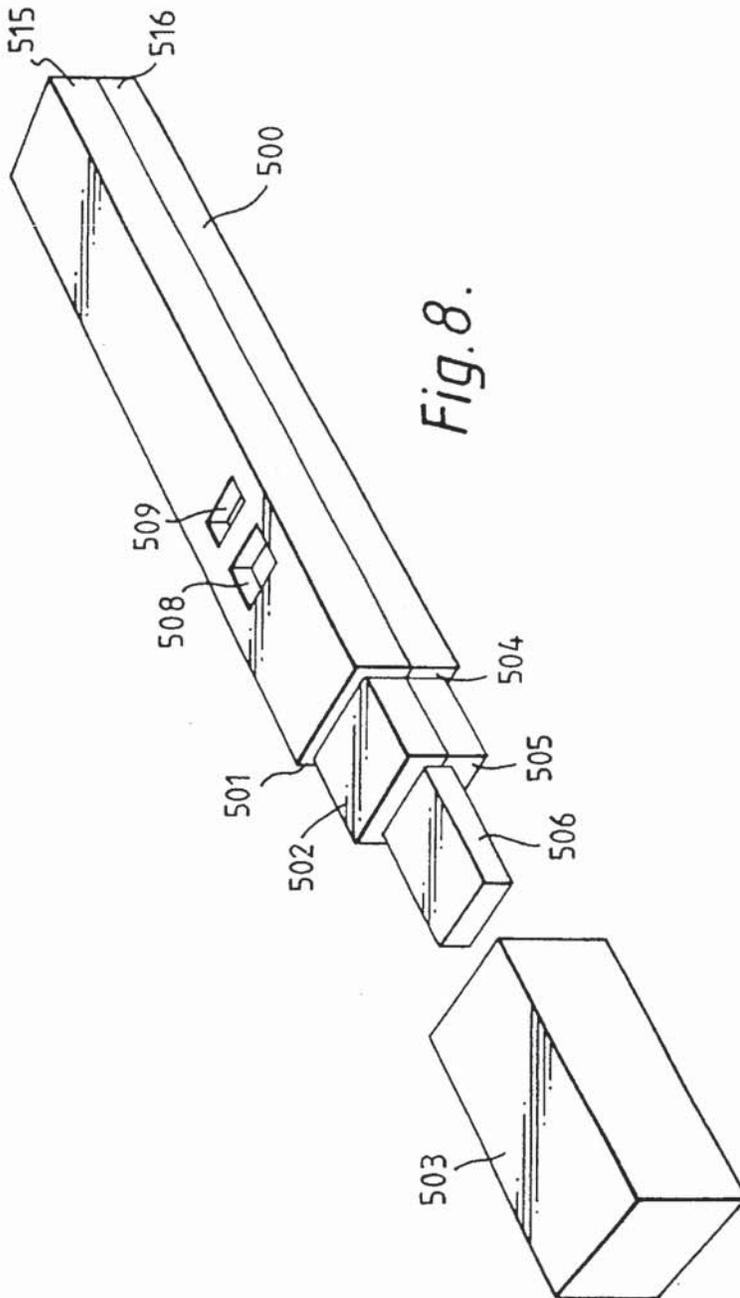


Fig. 8.

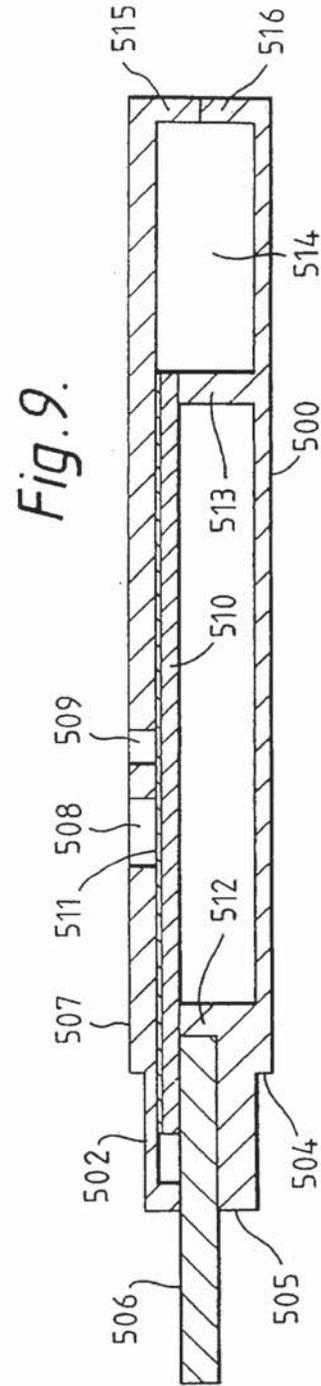


Fig. 9.

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.