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ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI,
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(54) Title: A METHOD AND APPARATUS FOR PRODUCING FINE CONCENTRATED AEROSOL

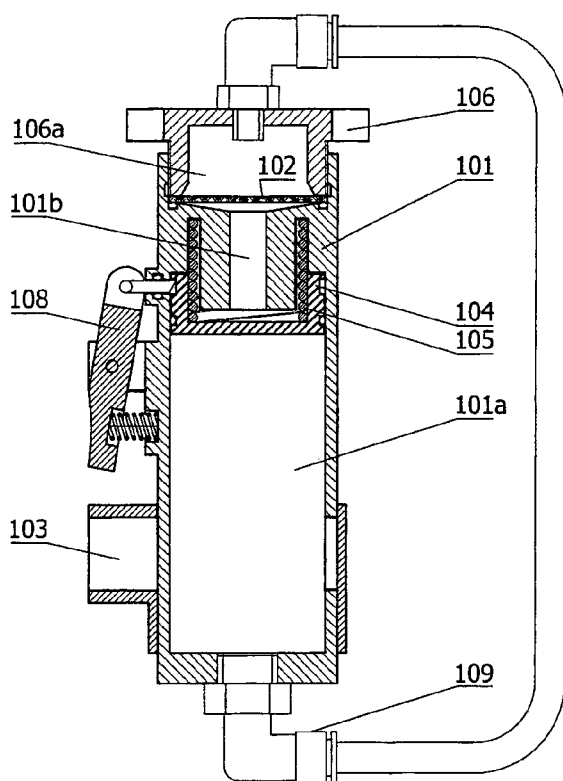


Fig.3

(57) Abstract: The invention relates to a method and apparatus for producing fine and concentrated aerosol from liquids, for various applications, by using rigid porous material, storage and easy streaming of the aerosol, (i.e. for inhalation), fast replacement of liquid carrier device and accuracy of output sprayed dose.



LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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A METHOD AND APPARATUS FOR PRODUCING FINE CONCENTRATED AEROSOL

5 **Field of invention**

The present invention relates to a method and apparatus enabling production of ultra fine and concentrated aerosol from liquids, for various applications, by using rigid porous material, enabling storage and easy streaming of the aerosol, (i.e. for inhalation), fast replacement of liquid carrier device and accuracy of output sprayed dose.

Background of invention

The efficiency and effectiveness of nebulizer technology depends on its ability to produce droplets of aerosol characterized by required parameters (i.e.: size, concentration etc.) since these parameters have a direct impact on the performance of the aerosolized material (i.e. therapeutic effect). Additional needs are to eliminate product loss during operation and to allow convenience of use.

From existing professional bibliography it is known that: Effective lung healing treatment requires a certain dose of medicine composed of particles sized 0.5 to 2 micrometer.

Prior art

U.S Patents

Patent Number		Date of Patent
4,743,407	Externally pressurized porous cylinder for multiple surface aerosol generation and method of generation	May 10, 1988
6530370	Nebulizer apparatus	Mar 11, 2003
5718222	Disposable package for use in aerosolized delivery of drugs	Feb 17, 1998
6070575	Aerosol-forming porous membrane with certain pore structure	Jun 6, 2000
6230706	Method and device for creating aerosol with porous membrane with certain pore structure	May 15, 2001

Patent Number		Date of Patent
5497763	Disposable package for intrapulmonary delivery of aerosolized formulations	Mar 12, 1996
5855564	Aerosol extrusion mechanism	Jan 5, 1999
7013894	Portable, handheld, pneumatic driven medicinal nebulizer	Mar 21, 2006
5379760	Position insensitive low resistance aspirator	Jan 10, 1995
6899322	Method and apparatus for production of droplets	Dec 31, 2001
7562656	Aerosol medication inhalation system	Sep 17, 2004
3762409	Nebulizer	Nov 3, 1970
D471626	Nebulizer	: Dec 10, 2001
RE30046	Nebulizer	Jul 17, 1979
5823179	Nebulizer Apparatus and method	Oct 20, 1998
5570682	Passive aspiratory nebulizer system	Nov 5, 1996
5685291	Nebulizer adapter system for premature babies	Nov 11, 1997

Existing nebulizers:

Pneumatic nebulizers have orifices of 500 micrometer and more and other means of separation (extraction) of large droplets, therefore the obtained aerosol is of low concentration, (Concentration = Quantity of droplets per volume), usually less than $10^7/\text{cm}^3$). Such low concentration increases the treatment time in order to achieve use of required dose. In addition there is a hardship to control the dose achieved by existing nebulizers, even some of the most advanced nebulizers entail a synchronization system between the aerosol supply and the respiration rhythm yet there is still aerosol loss and dose accuracy can hardly be maintained.

In the existing nebulizers a significant quantity of atomized liquid is lost in the process of preparing the aerosol due to "dead" volume that can never be sprayed as aerosol.

An additional disadvantage of the existing nebulizers is a mandatory use position (e.g. vertical) to allow proper device operation and to control the amount of the dose.

Another factor to be considered is the exposure of environment to the aerosol (i.e. medicine) while using the existing nebulizers. While patient uses a mask, tent or any other kind of disperser, there is an existing risk of medicine leakage that might be hazardous to environment.

To date the existing nebulizers of ultrasonic type do not allow spraying all kind of liquids since during their process the medicine absorbs ultrasonic energy and heats, which harms the medicine and can distort it. Such nebulizers require high rate supply
5 of external air for liquid cooling and streaming thus creating a relatively low concentrated aerosol (even though higher than the pneumatic type nebulizers) but no more than $10^8/\text{cm}^3$, in best conditions, therefore, the treatment time required, is still high.

The proposed technology resolves the above mentioned problems and overcomes the
10 above encountered disadvantages while offering additional advantages.

Summary of the invention

The proposed technology is intended for creating ultra fine aerosol by using rigid
15 porous material (1) (fig.1).

The ultra fine aerosol (0.3 to 1.1 micrometer of droplet size of the aerosol) is achieved due to specific parameters of the porous material, while the porous material acts as a pneumatic multi-nozzle atomizing system. The porous medium itself is in fact an integral system consisting of the following elements:

- 20 • The liquid (3) for spraying (been on the surface of the porous medium and/or partially absorbed in it)
- A large number of pores (2) (of sub-micron size) acting as nozzles.
- Gas (4) caged in those pores which are vacant of liquid.

The aerosol spraying is performed by instantaneously inducing pressure drop to the
25 thickness of the porous medium (for instance: when the medium is 'coin' shaped the differential pressure occurs between the two flat sides of the 'coin') . For example, when the porous medium (which contains the above mentioned liquid and gas) is in atmospheric pressure a sharp pressure drop is induced on one side of the medium (e.g. 600 to 900 mbar less than atmospheric pressure, depending on the porous
30 medium characteristics) (Fig.2b) . In this stage atomizing occurs as a result of the differential pressure (between the two sides of the medium) which causes the medium to act as a pneumatic multi-nozzle. The reason for the effect of pneumatic

multi-nozzle atomization is that the air (4) (Fig.1) which was caged in the internal volume of the porous medium releases itself in the direction of vacuum, causing the pores (2) (Fig. 1) to act as nozzles and spray the liquid (3) (Fig. 1) outside from the medium. The aerosol is then achieved on the side of the lower pressure (atomized side (102a)) (Fig2a) with no need for external (atomizing) gas supply.

The under-pressure mentioned above is produced in a chamber, whereas the porous medium is a part of the chamber.

According to the above technology, it is possible to achieve fine aerosol with high concentration (10^9 - 10^{11} /cm³) and more.

10 The same chamber in which the under-pressure (vacuum) is produced is also used for storing the aerosol, hereby referred to as "the vacuum accumulator", until the aerosol is required for use (i.e. inhalation), whereas the stability of the aerosol in the chamber depends on its concentration.

15 In order to take out aerosol (103) (Fig2c) from the vacuum accumulator, the pressure in the vacuum accumulator needs to be changed. For example, for an inhalator, an atmospheric pressure has to be produced in such a way that will allow the inhalation of the stored aerosol as a whole with no losses, dosed and repeatable, without need for any synchronization with the respiratory tract.

20 The vacuum accumulator element may also be used as a drying chamber depending on the relation between the volume of the accumulator chamber and the quantity of the droplets and on the overall parameters of the environment in vacuum accumulator (e.g. temperature, pressure, etc.). In such case dry aerosol can be obtained by the nebulizer (e.g. for purpose of dry particles inhalation, which is a new kind of dry-particle-inhaler that acts without pressurized gas).

25 Additional drying process can take place by the act of inhalation itself, when the inhaled air acts as drying agent.

The described nebulizer has the following advantages:

- The nebulizer can be operated in any environment and any position: upright, horizontal and even in outer space.
- 30 • Possible of being self sustained.

The porous element may also be used as a storage container for the liquid (i.e. medicine) prior to its conversion to aerosol (can be referred to as "pill"), when it is

soaked with a determined quantity of liquid or alternatively when it is normally dry but covered with a buffering (dry) layer (that is not transferable for liquid) packed together with a liquid container (that together with the porous medium form a “sandwich” like device) that has a mechanism of wetting the medium (e.g. by removing the buffering layer) which is performed before the atomizing effect (before the insertion of the “pill” into the nebulizer, or afterwards by an internal mechanism of the nebulizer).

When carried around by user (i.e. prior to atomization process), the “pill” is hermetically and sterilely sealed and packed.

10 The “pill” is designed to be used with specific nebulizer device. Matching or un-matching combinations can be created to allow or deny certain usage combinations.

Serving as a liquid container the “pill” can contain any desired liquid formulation (e.g. medicine, food supplement, natural sources, etc.) while the “pill” serves as a generic platform for carrying the liquid, ready to be converted into aerosol anytime when fed into a nebulizer device (i.e. for inhalation purposes).

The “pill” can be disposable. It is designed for easy replacement and discharge.

Description of the drawings:

20 Fig 1 describes: (1) - porosive material; (2) - nozzles (pores); (3) - liquid for spraying, (4) - gas

Figs .2a; 2b; 2c & 3 describe the nebulizer, in different stages: (2a) – when the nebulizer is in idle position, before aerosol is produced; (2b) – the nebulizer is in under-pressure production and aerosol production; (2c) – nebulizer during inhalation act.

Detailed description:

- Outer structure (101) containing the vacuum accumulator (101a). The vacuum accumulator's dimensions are determined according to the volume of aerosol required for each application. For example: to produce 30 mg of medical aerosol for local delivery to the lung or systematic delivery through the lung, a volume of 30 cc is required.

- The vacuum accumulator has a path (101b) through which the aerosol received from the porous material (102) enters the vacuum accumulator (101a).
 - The exit hole (103) for aerosol inhalation is externally closed by rotating cover.
 - Under-pressure effect can be generated either externally by a vacuum pump (for stationary use) or by an internal device of the nebulizer itself, for example, with the help of the cylinder pistol (104) that is moved by spring (105).
 - On the upper side of the device there is a place to insert the porous medium (102), which may be in the shape of a cylinder, disc, cup or the like, that if fixed or sealed to the device by cover (106), designed for fast opening/closing and has a duct (106b) connecting to environment or vacuum accumulator(101a).
- The location of the porous media in relation to the device can be on its upper side (as appears in the drawing) but can also be in the opposite (bottom side) or in any side of the device.

The material, structure and dimensions of the porous material (102) are determined according to the required aerosol characteristics for each required application. For example: the dispersing area determines the quantity of achieved aerosol.

Fig. 2a shows the nebulizer prepared for generating aerosol:

- spring (105) is compressed;
- piston (104) is captured in upper position with fixture (108);
- the porous medium (102) inserts to a place and fixed by cover (106);
- the exit hole for aerosol closed by rotating cover (103).

Fig. 2b shows the spraying nebulizer :

- piston (104) is - in lower position;
- vacuum accumulator (101a) is filled by aerosol.

Fig. 2c shows the nebulizer prepared for aerosol exploitation: rotating cover (103) connecting to environment.

Fig 3 shows the nebulizer with tube (109) for supply air in spraying stage from vacuum accumulator (101a) to a duct (106b) to increase aerosol capacity by increasing dispersing air. Introducing additional dispersing air causes increase of the differential pressure.

What is claimed:

1. A method to produce ultra fine and highly concentrated aerosol from liquid is
5 performed by instantaneously inducing differential pressure drop (atmosphere – vacuum) to the thickness of the porous medium with liquid partially absorbed in it, which causes the pores of the porous medium to act as a pneumatic multi-nozzle and immediately produce aerosol from the lower pressure side of the medium, with no need for external (atomizing) gas supply, the soaked liquid when sprayed, produces
10 the desired treatment quantity in an aerosol form (wet or dry) (i.e. product) used for local delivery (e.g. when the lung area is a target) or for systemic therapeutic when the product reaches the blood stream through the deeper levels of the lungs.
2. The method of aerosol production as defined in claim 1 requires introducing differential pressure drop effect that can be achieved by any known vacuum
15 generating method (e.g. vacuum pump, piston etc.).
3. The method of aerosol production as defined in claim 1 requires preparation of the porous medium acting as pneumatic multi-nozzle atomizing system which is performed by wetting the porous medium in a manner that some of the pores remain vacant of liquid.
- 20 4. The method as defined in claim 1 when the produced aerosol is held in vacuum (referred to as 'vacuum accumulator') is then transferred to hermetic chamber for the purpose of storage for easy use at a later stage (i.e. inhalation).
5. The method of aerosol production as defined in claim 4 when the vacuum accumulator may also be used as a drying chamber. In such case dry aerosol is
25 obtained by the nebulizer for purpose of dry particle inhalation, that acts without pressurized gas.
6. A nebulizer apparatus for producing either concentrated fine wet aerosol or concentrated dry aerosol from liquids comprises:
 - A device containing the vacuum accumulator whose dimensions are
30 determined according to desired treatment parameters (dry or wet aerosols, dosage, etc.), also used for stable storing of the aerosol before usage, whereas aerosol stability in the chamber depends on its concentration and other environment parameters (such as temperature, pressure, etc.).

- A rigid porous material acting as a pneumatic multi-nozzle atomizing system, comprises:
 - a. The liquid for spraying been on the surface of the porous medium and/or partially absorbed in it.
 - 5 b. A large number of pores of determined sub-micron size acting as nozzles.
 - c. Gas which is caged in those pores that are vacant of liquid.
 - A path through which the aerosol received from the porous material enters the vacuum accumulator.
 - An element for creating immediate differential pressure drop in any known
 10 vacuum producing method (e.g. by piston and spring, vacuum pump, etc.) to the thickness of the porous medium with liquid partially absorbed in it.
 - An outlet hole for inhalation, closed by a cover.
 - On either side of the device there is a place to insert the porous medium that is fixed or sealed to the device by cover, designed for fast opening-closing and has
 15 a duct connecting to environment of vacuum accumulator.
7. The apparatus as defined in claim 6 when the porous element is removable, and the device has mechanism to allow fast feed and replacement of the porous element. This removable element when soaked with certain quantity of liquid (i.e. medicine) is used as a "pill" containing medication. The "pill" is carried by the user
 20 and kept sterile by its packaging until it is ready for use (i.e. inhalation).
8. The apparatus as defined in claim 7 which is a porous medium in the shape of a cylinder, disc, cup or the like, structure, material, design and dimensions of which are determined according to the required atomizing parameters for each specific use. For instance: the atomizing area determines the quantity of aerosol achieved.
- 25 9. The apparatus as defined in claim 6 includes a tube connected from vacuum accumulator to a duct of cover for increasing aerosol capacity by increasing differential pressure in the atomizing stage.
10. The apparatus as defined in claim 6 in which air located in vacuum accumulator during the stage of vacuum production passes to the side of positive
 30 pressure of the porous medium and passes again through the porous medium and increases the atomizing capacity and together with this aerosol enters the vacuum

accumulator in a sterile manner and brings pressure in the vacuum accumulator close to atmospheric pressure.

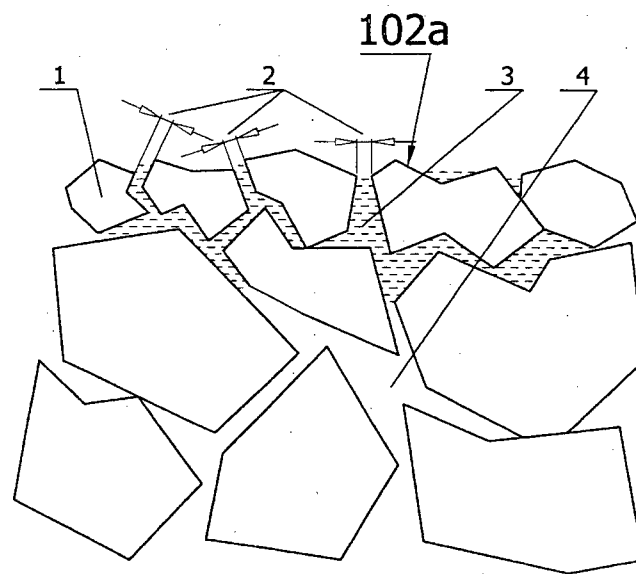


Fig.1

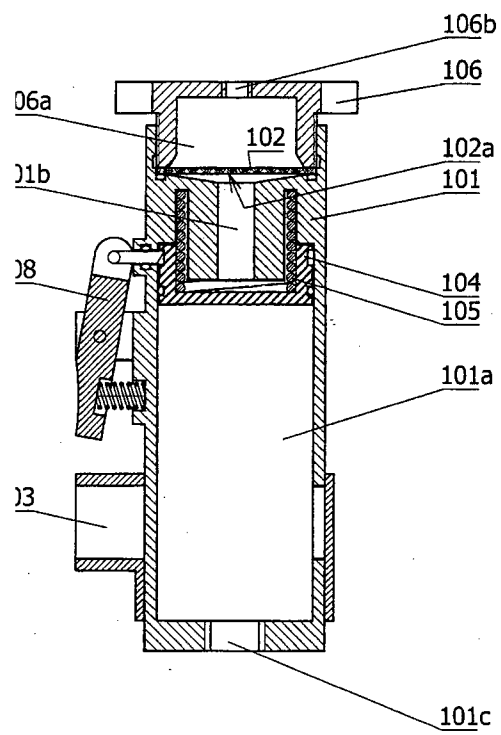


Fig.2a

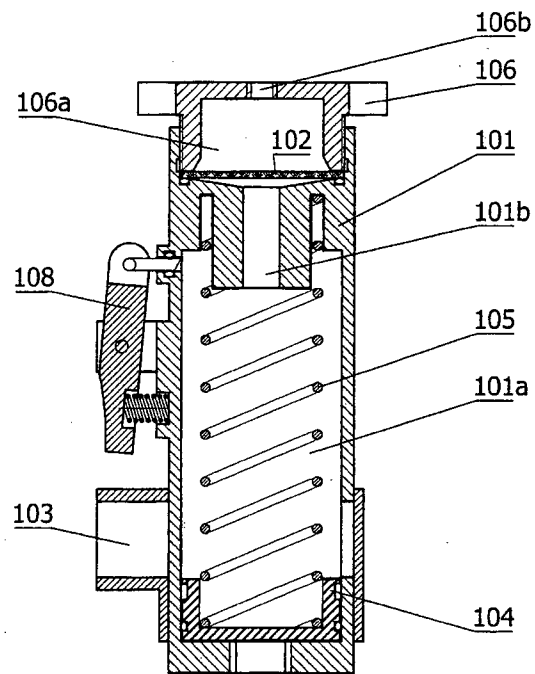


Fig.2b

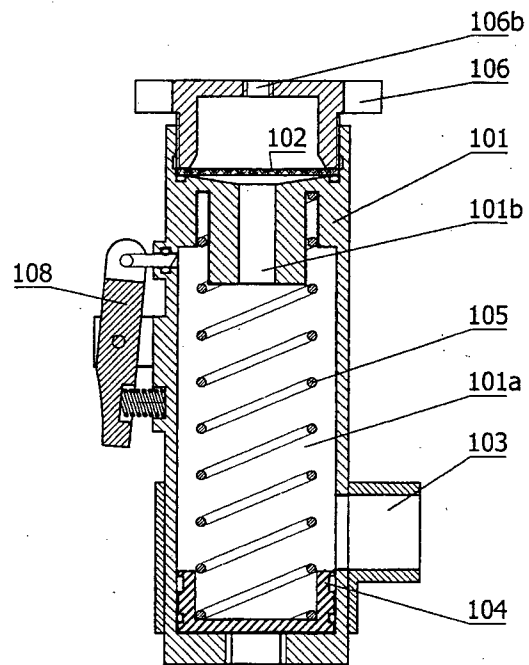


Fig.2c

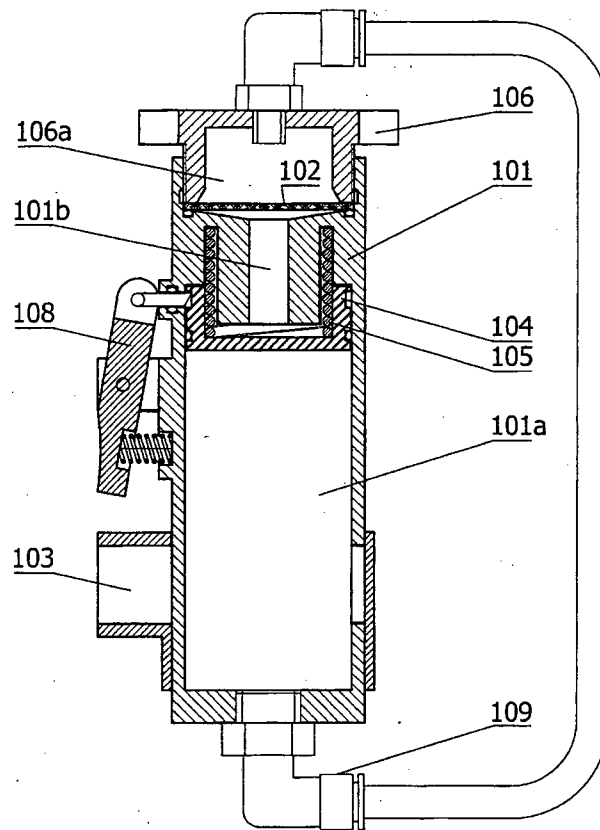


Fig.3

INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2011/000038

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61M11/00 A61M11/02 A61M11/06
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 915 378 A (LLOYD LESTER J [US] ET AL) 29 June 1999 (1999-06-29) figures 3,4 claim 14 column 1, line 17 column 3, line 11 - line 24 column 4, line 35 - line 39 column 22, line 65 - column 23, line 11 -----	1-3
X	WO 00/50111 A1 (VOGES ROBERT MARTIN [US]) 31 August 2000 (2000-08-31) claims 42-44 page 9, line 2 - line 4 page 21, line 25 - line 28 ----- -/--	1



Further documents are listed in the continuation of Box C.



See patent family annex.

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Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2011/000038

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 301 664 A (SIEVERS ROBERT E [US] ET AL) 12 April 1994 (1994-04-12) figure 4 column 6, line 30 - column 7, line 9 -----	1-10
A	WO 01/66064 A2 (ARADIGM CORP [US]; RUSKEWICZ STEPHEN JOHN [US]) 13 September 2001 (2001-09-13) page 15, line 19 - line 29 -----	1-10

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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