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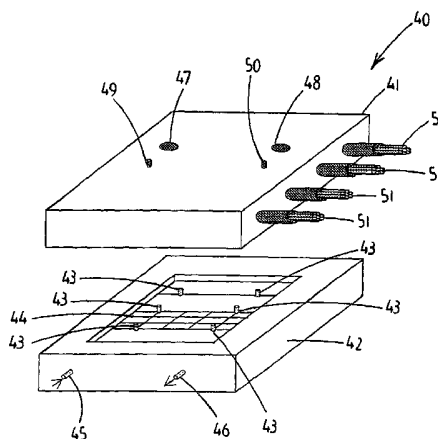
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(54) Title: SYSTEM FOR PERFORMING A CHEMICAL REACTION ON A PLURALITY OF DIFFERENT MICROREACTORS



(57) Abstract: A system for performing at least one chemical reaction on a plurality of different microreactors comprises a device having positioning means designed for at least temporarily receiving, at a fixed position within the device, of at least one of the plurality of different microreactors. The device comprises a set of device communication means, each device communication means being designed for communicating a specific quantity with the at least one microreactor at a specific location relative to the microreactor received in fixed position in the said device. The system further comprises the plurality of microreactors, each one of the microreactors comprising a subset of microreactor communication means for communicating a subset of the said specific quantities with a corresponding subset of the device communication means, when the microreactor is received in fixed position in the device. Each particular microreactor communication means for communicating a particular specific quantity is positioned on an identical location relative to the device on each of the microreactors comprising the particular microreactor communication means, when positioned in the device.

**SYSTEM FOR PERFORMING A CHEMICAL REACTION ON A
PLURALITY OF DIFFERENT MICROREACTORS**

The invention relates to a system for performing at least one chemical reaction on a plurality of different microreactors. Further, the invention relates to a device for such a system and a microreactor for use in such a system.

5 DE 199 28 410 A1 describes a device for operating a laboratory microchip. The device comprises a first unit, in which a microchip can be positioned. Further, the device comprises a second unit which is releasably mounted to the first unit. The second unit comprises a supply device comprising outputs for supplying substances to the
10 microchip and electrodes for establishing electrical connections towards the microchip. The second unit further comprises an intermediate device, which comprises channels and guide throughs for connecting the outputs supplying the substances and the electrodes to respective inlets and electrodes comprised in the microchip. Further,
15 the intermediate device can comprise channels for supplying a pressure medium such as a gas or a fluid to the microchip for moving the substances on the microchip. Thus, all connections between the supply device and the microchip are established via the intermediate device. As the intermediate device is releasably mounted to the
20 second unit, a different intermediate device can be mounted in case that a different microchip is placed in the device. For each type of microchip having a different geometrical outline of supply openings for supplying substances to the chip and a different geometrical outline of electrodes on the chip, a different intermediate device is
25 available to establish connections between the supply device and the openings and electrodes on the respective chip.

Consequently, adapting the device for use with a different type of microchip is time consuming as the intermediate device which is mounted in the device needs to be removed after which another
30 intermediate device is to be mounted. As such removing and mounting procedure will normally be followed by testing, to test whether the

intermediate device which has been mounted is of the correct type, and whether all connections between the supply device and the intermediate device are free of leakage, adaptation of the device to a different type of microchip is time consuming. Also, this will
5 involve human interaction and human supervision which further makes the device unsuitable for use in a highly automated, robotic environment. A further problem is that the device might be contaminated, in case that an incorrect intermediate device is mounted, causing chemical substances to be released into the device,
10 as channels in the intermediate device might not match to openings in the microchip. Apart from contamination, also further damage to the device might occur, when the contaminating substance gets into contact with one or more of the electrodes, which might lead to electrolyse or other unforeseeable consequences.

15 Further, US-6 001 311 describes an apparatus for diverse chemical synthesis using a two-dimensional array. The apparatus includes a head assembly having an array of nozzles, wherein each nozzle is coupled to a reservoir of liquid reagent. Further, the apparatus comprises a base assembly having an array of reaction wells
20 and a transport mechanism for aligning the reaction wells and selected nozzles in a longitudinal X-direction for the deposition of liquid reagent into selected reaction wells. The apparatus however is only suitable for a single type of arrays.

The invention provides a system for performing at least one
25 chemical reaction on a plurality of different microreactors obviating the problems of the prior art.

To achieve this goal, the system according to the invention comprises a device having positioning means designed for at least temporarily receiving, at a fixed position within the device, of at
30 least one of the plurality of different microreactors, the device comprising a set of device communication means, each device communication means being designed for communicating a specific quantity with the at least one microreactor at a specific location relative to the microreactor received in fixed position in
35 the said device, the system further comprising the plurality of microreactors, each one of the microreactors comprising a subset of microreactor communication means for communicating a subset of the said specific quantities with a corresponding subset of the device

communication means, when the microreactor is received in fixed position in the device, wherein each particular microreactor communication means for communicating a particular specific quantity is positioned on an identical location relative to the device on each of the microreactors comprising the particular microreactor communication means, when positioned in the device.

The device communication means for communicating quantities, such as substances, electrical signals, optical signals, electrical energy or any other quantity are all located on standardized positions. Each device communication means is designed for communicating a quantity with a microreactor communication means which can be comprised in one or more of the microreactors. As different microreactors might require communication of different quantities, each one of the microreactors comprises a set of microreactor communication means for communicating a subset of the quantities with a corresponding subset of the device communication means, when the microreactor is received in fixed position in the device. As each particular microreactor communication means is positioned on an identical location on each of the microreactors comprising the particular microreactor communication means, when positioned in the device, the particular microreactor communication means will communicate with the corresponding device communication means comprised in the device.

As a simple example to illustrate this principle, assume that the device comprises five device communication means, indicated as A, B, C, D and E. Each of these device communication means is designed for communicating a different specific quantity with a microreactor received in fixed position in the device. The device communication means are each designed for communicating a specific quantity which are microreactor communication means comprised in one or more of a plurality of different microreactors. By way of example, device communication means A is designed for communicating with microreactor communication means a, device communication means B is designed for communicating with microreactor communication means b, and accordingly, device communication means C, D and E are designed for communicating with microreactor communication means c, d and e, respectively. As an example, a first one of the microreactors only requires communication of a corresponding quantity with device

communication means A and B. Thus, this microreactor at least comprises microreactor communication means a and b. A second microreactor which differs from the first microreactor, requires communicating specific quantities with device communication means A, C, and D. Thus, this second microreactor at least comprises microreactor communication means a, c and d. Thus, the first microreactor comprises a subset comprising microreactor communication means a and b, while the second microreactor comprises a subset comprising a, c, and d. For both the first and second microreactor, microreactor communication means a is positioned on an identical location relative to the device, the respective microreactor being positioned in the device. Consequently, for both the first and second microreactor, microreactor communication means a will communicate with device communication means A. The first microreactor further comprises microreactor communication means b and accordingly, the second microreactor comprises microreactor communication means c and d. For all microreactors comprising microreactor communication means b, c and d, the respective microreactor communication means is positioned on an identical location relative to the device, when the microreactor is positioned in the device, and thus microreactor communication means b, c and d, as far as they are comprised in the subset of microreactor communication means comprised in one of the microreactors, will be able to communicate with device communication means B, C and D, respectively.

Herein, a chemical reaction can comprise any kind of chemical process including catalytic and enzymatic reactions, homogeneous and heterogeneous reactions, analysis, syntheses, mixing, separation, decomposition, detection of chemical substances or properties and others as appreciated in the art. The microreactor can comprise a chip, such as a microchip which can be made of any suitable material, such as glass, a ceramic, etc. The chip can comprise an array of reaction wells, each reaction well for performing a chemical reaction. It is possible that identical reactions are performed in all reaction wells, however it is also possible that different reactions are performed in some or all of the wells comprised in the array. Also it is possible that the chip comprises a flowpath for guiding a flow of a substance in or on the chip. Further, a plurality of different microreactors herein refers to a plurality of

microreactors which are not identical to each other. Differences can be found in many fields, such as a number of reaction wells or reaction channels found in a microreactor, different provisions for inputting and/or outputting different or identical substances, or
5 different quantities of the substances to the microreactor, the microreactors can be designed for different types of reactions, for different types of environmental conditions (such as temperature, pressure, etc.), different sizes of the microreactors, or any other difference.

10 Different reactions in this document advantageously refer to reactions that make use of the same substances but differ from each other in terms of e.g. concentrations or quantities of these substances, different catalysts, different reaction conditions, such as reaction time, pressure, pH, and/or a difference in another
15 reaction parameter. Alternatively it is of course also possible within the scope of the invention that the different reactions differ from each other as the reactions involve a different reaction mechanism or different substances, such as different input substances (reactants) which are supplied to the reactions and/or different
20 output substances (reaction products) which are generated in the reactions.

The quantity can comprise any entity which is to be exchanged with the microreactor before, during or after the reaction taking place, the quantity comprising matter (such as substances), energy
25 (such as electric energy), or information (such as electrical data signals); or a combination of such items.

The device communication means of the set of device communication means can all be designed for communicating different quantities with a microreactor, however, it is also possible that the
30 device communication means are designed for communicating the same quantity, such as a same chemical substance, or a same quantity but showing a different intensity, flow, power, pressure or any other difference.

Thus, according to the invention the device can be used with
35 each of the plurality of different microreactors, and the microreactors can be exchanged in a quick and simple manner, requiring no additional adaptations or modifications of the device. As all microreactor communication means have a standardized position,

positioning of the microreactor communication means and device communication means respectively to each other is automatically guaranteed, when a microreactor is positioned in the device. This eliminates a risk of human errors, as no adaptations of the device are required when installing a different microreactor, which also minimizes a need for human interaction and supervision, and thus allows a higher degree of automation, such as robotisation. As a consequence, various, possibly different tests, reactions, or projects involving multiple reactions can be sequentially performed at a high speed requiring minimum human interaction.

Advantageously, at least one of the device communication means and at least one of the corresponding microreactor communication means comprised in at least one of the microreactors are designed for communicating a substance with the microreactor, when positioned in the device. "Communicating a substance" comprises any kind of inputting, outputting or providing any other possibility for an exchange of matter, such as by means of diffusion. The device communication means can comprise a gas outlet means and the microreactor communication means can comprise a gas inlet port. Thus, a gas can be supplied by the gas outlet means to a microreactor comprising the gas inlet port.

Advantageously, the device communication means can comprise a gas inlet means, and the microreactor communication means can comprise a gas outlet port.

Further, the device communication means can comprise a liquid outlet means and the microreactor communication means can comprise a liquid inlet port, allowing propelling of a liquid to a microreactor.

The device communication means can comprise a liquid inlet means for introducing one or more liquids to the microreactor, and the microreactor communication means can comprise a liquid outlet port, for outputting one or more liquids from the microreactor.

Advantageously, at least one of the device communication means and at least one of the corresponding microreactor communication means comprised in at least one of the microreactors are designed for establishing an electrical connection between the device and the microreactor, when positioned in the device. Thus, the device communication means advantageously comprising electrical connection means, are able to establish an electrical connection with the

microreactor communication means, advantageously comprising an electrical connection port. Via the electrical connection, electrical energy and / or electrical signals comprising data can be communicated between the microreactor and the device.

5 Advantageously, at least one of the plurality of microreactors comprises sensing means for sensing a parameter on or in the microreactor, the sensing means being connected to at least one of the electrical connection ports. Thus, the sensing means can sense a parameter on or in the microreactor, while a signal from the sensing
10 means, such as an analogue signal or a digital signal is directed via one of the electrical connection ports to the device. Also it is possible that via the electrical connection ports electrical power, such as a supply voltage is provided to the sensing means. In this manner, for example a temperature can be sensed on or in the
15 microreactor, in case that the sensing means comprises a temperature sensor.

Advantageously, at least one of the plurality of microreactors comprises an actuator which is connected to one of the electrical connection ports. Thus, electrical connections to an actuator
20 comprised in at least of the plurality of microreactors can be made via one of the electrical connection ports.

The actuator can comprise a microreactor temperature conditioner, such as a heater comprised in the microreactor. The microreactor temperature conditioner can be designed for
25 conditioning, or altering a temperature in or on the microreactor as a whole, or in a temperature zone of the microreactor. Further, the actuator can comprise a pump, such as an electro-osmotic pump. Of course, also other types of pumps are possible, such as a mechanical pump or a pressure driven pump, which can be provided with a pressure
30 by a medium, such as a gas, which can be provided by a gas outlet means comprised in the device to a gas inlet port, comprised in a microreactor comprising such pump.

Advantageously, the device comprises device sensing means and/or device actuators which are positioned in a fixed position with
35 regard to the device communication means. As the device sensing means and/or device actuators are positioned in a fixed position, all microreactors which require use of a particular device sensing means and/or device actuator can apply the same, implying that

manufacturing costs of microreactors can be reduced, as sensing means and/or actuators which are common to different types of microreactors can be implemented as device sensing means and/or device actuators respectively, which are comprised in the device.

5 The device actuators can comprise pressure adaptation means for adapting a pressure in a pressure zone comprised in the device. Further, the device actuators can comprise temperature conditioning means for conditioning a temperature in a temperature zone comprised in the device.

10 Advantageously, the device further comprises data processing means for processing sensing means data and/or device sensing means data and/or for controlling actuators and/or device actuators. The device can further comprise a communication interface connected to the dataprocessing means for communication with a dataprocessing
15 device. Thus, (device) sensing means data and/or (device) actuator data can be processed by the processing means, allowing implementation of control loops, datalogging, and other control functions which are known per se and via the communication interface it is possible to send data to a dataprocessing device, such as an
20 external computer.

Advantageously, each of the plurality of microreactors comprises microreactor identification means for identifying the microreactors and in that the device comprises microreactor identification readout means for reading out an identification of a
25 microreactor positioned in the device. Thus, the device can identify the microreactor which is positioned in the device, thus eliminating errors caused by placement of an incorrect microreactor in the device. The identification means can be arranged to identify a type of microreactor, enabling to identify different microreactors,
30 however it is also possible that the identification means are further able to identify each microreactor individually, even if of the same type, by for example reading out a serial number.

Advantageously, the device further comprises at least one external communication means for communicating at least one of the at
35 least one quantities with an external device. By the external communication means at least one of the quantities can be communicated with an external device. Thus, quantities can be communicated with the device from an external device, and from the

device, the quantity can be communicated to a microreactor positioned in the device. This can simplify the device as use of existing external devices can be made. Existing liquid dosing systems, gas supply systems, and many others, can be applied for providing (part of) the communication with a microreactor. The external communication means can for example comprise an external gas inlet means and/or gas outlet means, a liquid inlet means and/or liquid outlet means. The external communication means can be connected to one or more respective device communication means directly, such as for example via a channel, however it is also possible that control functions, implemented by one or more valves, pumps, etc. are connected between the external communication means and the device communication means. Also it is possible, for example in case that the device is able to simultaneously receive a plurality of microreactors, that an external communication means is coupled via a multiplexing or distribution means, which might be known per se to a plurality of device communication means for enabling communication between the plurality of microreactors received in the device and the external device. As the external communication means are positioned in a fixed position with respect to the device, usage of different external devices, such as robots might be made, as the standardized position of the external communication means with regard to the device results in a standardized interface between the device and the external devices. Thus, according to the invention, interchangeability is achieved not only between the different microreactors and the device, but also between the device and a variety of external devices making use of the external communication means which results in the situation that the plurality of different microreactors can, making use of the device, easily be operated by standard or custom made, interchangeable external devices. Thus, in fact a versatile "coupling" between a macroworld comprising the external devices and a microworld, comprising the microreactors has been achieved which allows the macroworld devices to be easily and flexibly applied with a variety of different microreactors.

Advantageously, the device further comprise a housing, for enclosing at least one microreactor when positioned in the device. Thus, environmental conditions such as pressure, high temperature, or a clean atmosphere showing a low amount of dust particles, or an

atmosphere comprising a specific gas can easily be created around the microreactor positioned in the device.

The housing can comprise a plurality of compartments, each compartment for enclosing at least one microreactor when positioned in the device. Thus, different environmental conditions, if required, can be achieved for various microreactors which are positioned in the device simultaneously.

Advantageously, the microreactor comprises a layered structure comprising one or more layers chosen from a group of layers comprising at least one electrical layer, at least one reactor layer and at least one inlet/outlet port layer. The electrical layer which comprises electrical connection means for establishing electrical connections with the microreactor, can comprise a plastic or other insulation material, a conductor such as copper or an other metal for establishing electrical connections, and possibly electronic components such as semiconductor components, which can be placed on a (e.g. ceramic) substrate. The reaction layer for performing the reaction preferably comprises a glass or a plastic. The inlet / outlet port layer comprises at least one inlet port and/or outlet port of the microreactor. Also it is possible that one or more inlet and / or one or more outlet ports are comprised in the reactor layer. Because of the layered structure, different microreactors can be developed in a very short time, as a microreactor can be built up from one or more layers comprised in the group of layers. Thus, the microreactor can be assembled by choosing one or more particular electrical, reactor and / or inlet / outlet layers from the group of different layers and assembling the layers to form a microreactor. The invention further comprises a device for a system according to the invention. Also, the invention comprises such a device holding a plurality of microreactors. The device can comprise microreactor identification means for identifying a microreactor or type of microreactor positioned in the device.

Further, the invention comprises a microreactor for use in a system according to the invention.

Further features and advantages of the invention will become clear from the appended drawing in which a non-limiting embodiment of the invention has been depicted, in which:

Fig. 1 highly schematically shows a top view of a set of device communication means;

Fig. 2a-2d highly schematically show a top view of different microreactors according to the invention; Fig. 3 shows a highly schematic, perspective view of the device according to the invention;

Fig. 4 shows a highly schematic, perspective view of a microreactor according to the invention.

Fig. 1 shows a set of device communication means 1, comprised in a device (not shown). The device communication means 1 comprise a gas outlet means 10, a gas inlet means 11, a liquid outlet means 12, a liquid inlet means 13, and electrical connection means 14, 15, 16 and 17. Each of the set of device communication means 1 is designed to communicate a quantity with a microreactor received in the device. The gas outlet means 10 is designed for supplying a gas to a microreactor, the gas inlet means 11 is designed for transporting a gas from the microreactor, the liquid outlet means are designed for supplying a liquid to the microreactor, and the liquid inlet means 13 are designed for transporting a liquid from the microreactor. The electrical connection means 14, 15, 16, 17 also each have a designated purpose, for example electrical connection means 14 is designed for reading out a signal from a temperature sensor comprised in a microreactor, electrical communication means 15 is designed for reading out a signal from a pressure sensor comprised in a microreactor, electrical communication means 16 is designed for supplying a high voltage to an actuator, such as an electro-osmotic pump, and electrical communication means 17 comprises a common grounding connection.

For illustrative purposes, gas outlet means 10, gas inlet means 11, liquid outlet means 12 and liquid inlet means 13 have been indicated with a circular symbol. Likewise, electrical connection means 14, 15, 16 and 17 have been indicated with a square symbol. These shapes are for illustrative purpose only. It will be clear to a person skilled in the art that the device communication means shown can have any suitable size, shape and construction. It is for example possible that device communication means of the set of device communication means 1 have different sizes, also it is possible that for example two device communication means of a same type, such as

for example two gas outlet means are comprised in the set of device communication means, each of the gas outlet means being designed for supplying a different type of gas, or supplying a different flow of a similar or same gas. The device communication means can thus have any suitable dimensions and shapes. As shown in Fig. 1, the device further comprises microreactor positioning means which are highly schematically indicated by 18, for positioning a microreactor in the device. The positioning means 18 can, instead of the positioning means, as schematically indicated in Fig. 1, have any suitable shape or construction, such as locator pins, etc.

The device communication means 1 shown in Fig. 1 are each designed for communicating a specific quantity, such as in this example a gas, a liquid, a temperature sensing signal, a pressure sensing signal, a high voltage, or a grounding signal with a microreactor 20, 21, 22 and 23 of the plurality of microreactors 20, 21, 22, 23, shown in Fig. 2a-2d. Each of the microreactors 20, 21, 22, 23 comprises a subset of microreactor communication means 30, 31, 32, 33, 34, 35, 36 and 37, which is designed for communicating with a respective device communication means 10, 11, 12, 13, 14, 15, 16 and 17 as shown in Fig. 1. Fig. 2a shows, by way of example, microreactor 20, comprising a subset of microreactor communication means, in this example microreactor communication means 31 comprising a gas outlet port and microreactor communication means 32 comprising a liquid inlet port. As microreactor 20 does not require any of the other microreactor communication means 30, 33, 34, 35, 36 and 37, this can be left away on microreactor 20. Thus, liquid-inlet port 32 and gas outlet port 31 are designed to communicate with liquid outlet means 12 and liquid inlet means 11 respectively as shown in Fig. 1. Consequently, liquid inlet port 32 and gas outlet port 31 are positioned on the microreactor 20 in such a way that, when microreactor 20 is positioned in the device by positioning means 18, liquid inlet port 32 and gas outlet port 31 communicate with liquid outlet means 12 and gas inlet means 11, respectively. Likewise, Fig. 2b shows a microreactor 21 comprising microreactor communication means 30, 31, 34, 35 and 37. Thus, Fig. 2b shows a microreactor 21, comprising a different subset of the microreactor communication means 30, 31, 32, 33, 34, 35, 36 and 37, compared to microreactor 20 shown in Fig. 2a. Microreactor communication means 30 comprising a gas

inlet port is designed for communicating with gas outlet means 10 shown in Fig. 1, Similarly, microreactor communication means 34, 35 and 37 are designed for communicating with device communication means 14, 15 and 17, when microreactor 21 is positioned by the position means 18, in the device. As an alternative to the example described, it is possible that the electrical connection means and corresponding electrical connection ports comprise pins and recesses for receiving the pins, the pins and recesses serving as positioning means for positioning the microreactor.

Fig. 2c again shows another microreactor 22 comprising microreactor communication means 30 and 31, comprising a gas inlet port and a gas outlet port respectively. Microreactor 22 has a different size if compared to microreactor 20, 21 and 23, which will be described below. However, microreactor communication means 30 and 31 are positioned on microreactor 22 in such a way that, when microreactor 22 is positioned by the positioning means 18 in the device, microreactor communication means 30 and 31 are able to communicate with device communication means 10 and 11, respectively.

Microreactor 23, shown in Fig. 2d, comprises microreactor communication means 30, 34, 36 and 37. As will be clear from the description regarding Fig. 2a, Fig. 2b and Fig. 2c, microreactor communication means 30, 34, 36 and 37 are designed for communicating with device communication means 10, 14, 16 and 17, respectively, when microreactor 23 is positioned by the positioning means 18 in the device. Thus, each one of the microreactor communication means 30, 31, 32, 33, 34, 35, 36, 37 is positioned on an identical location for all microreactors 20, 21, 22, 23 comprising the particular microreactor communication means 30, 31, 32, 33, 34, 35, 36, 37, such that when the particular microreactor 20, 21, 22, 24 is positioned by the positioning means 18 in the device, the particular microreactor communication means 30, 31, 32, 33, 34, 35, 36, 37 is able to communicate with the respective device communication means 10, 11, 12, 13, 14, 15, 16, 17 comprised in the device. For example, microreactor communication means 31 is positioned on an identical location relative to the device, when the microreactor is positioned in the device, for microreactors 20, 21 and 22.

It will be clear that the microreactors can have any suitable shape and suitable dimensions. Further it will be clear that the

microreactors 20, 21, 22, 23 comprise further elements, such as reactor channels, one or more reactor wells, etc. which are not shown in Fig. 2a-2b. The microreactor communication means can, next to or instead of being positioned on a top face of the microreactor as indicated in fig. 2a - 2d, also be positioned on or in any other part of the microreactor. It is for example possible that the microreactor communication means are placed on or in a bottom face or a side of the microreactor. A gas inlet port, a gas outlet port, a liquid inlet port and/or a liquid outlet port can for example be positioned on the top face, and electrical contact means can be positioned on one or more side faces, while a device actuator, such as a heater is for example positioned in the device in a location which is below the microreactor when positioned in the device.

The microreactors can comprise materials such as a glass, a ceramic, a metal or a plastic. Also it is possible that the microreactors comprise various materials, such as a plastic, as glass and a silicon. In this case, the plastic can be used for a housing or outer part of the microreactor, the glass can be used for parts of the microreactor which are in contact with one or more chemical substances in the microreactor, and the silicon can be used for semiconductor sensing devices, actuators and communication devices comprised in the microreactor.

Fig. 3 shows a device 40, comprising an upper part 41 and a lower part 42. The lower part 42 comprises positioning means, in this example a plurality of locator pins 43 for positioning one or more microreactors in the device. For that purpose, the microreactors (not shown) can be equipped with recesses, openings, holes or other mechanical provisions for co-operating with the locator pins 43. Further, the lower part 42 comprises a plurality of heating and/or cooling zones indicated by 44. The heating and/or cooling zones 44 provide a local heating and/or cooling to (a part of) one or more microreactors. The lower part 42 is provided with an external cooling input 45 and an external cooling output 46 for supplying a cooling medium to (part of) the heating and/or cooling zones 44. The upper part 41 of the device 40 comprises an external liquid input means and an external liquid output means 48. The external liquid input means 47 is connected via one or more channels (not shown) to one or more liquid outlet means (not shown) for supplying a liquid to a liquid

inlet port on a microreactor, when positioned in the device 40. Similarly, external liquid outlet means 48 is connected via one or more respective channels (not shown) to one or more liquid inlet means (not shown) each liquid inlet means for transporting a liquid from a liquid outlet port in a microreactor, when positioned in the device. Similarly, external gas inlet means 49 and external gas outlet means 50 are coupled via one or more respective channels to gas outlet means and gas inlet means, respectively, in the device, for transporting a gas to a gas inlet port, respectively from a gas outlet port comprised in a microreactor, when positioned in the device 40. The gas and/or the liquid can be propelled to and from the microreactor in any suitable way, such as by means of a pressure driven flow, a constant forced flow, etc. Also, the inlet means and outlet means can comprise any suitable means, such as one or more micropipettes, injection needles, etc. Further, the upper part 41 of the device 40 comprises electrical connections 51 comprising power supply lines, communication interface lines for communication with a dataprocessing device such as a personal computer.

When one or more microreactors are received in the lower part 42 of the device 40, and positioned by the locator pins 43, the upper part 41 is placed on top of the lower part 42. The upper part 41 and / or the lower part 42 can comprise fixation means (not shown) which can be known per se, for fixation of the upper part 41 and lower part 42 relative to each other, when the upper part 41 has been placed on top of the lower part 42. As the upper part 41 comprises a plurality of device communication means (not shown), the plurality of device communication means is available for communication with microreactor communication means comprised in the one or more microreactors positioned in the device 40. Thus, when the upper part 41 is placed on top of the lower part 42, each device communication means is able to communicate a specific quantity with the at least one microreactor at a specific location relative to the microreactor received in fixed position in the device. Of coarse, it is also possible that one or more device communication means are comprised in the lower part 42, next to or instead of the device communication means as described.

The device communication means in this example comprise liquid inlet means, liquid outlet means, gas inlet means, gas outlet means (all not shown). Further, the device communication means can comprise

electrical connection means which are designed for establishing an electrical connection with an electrical connection port comprised in a microreactor positioned in the device. The electrical connection means can establish electrical connections with sensors, such as a temperature sensor or a pressure sensor, or with an actuator, such as a temperature conditioner or a pump, such as an electro-osmotic pump, comprised in the device. It is possible that the electrical connection means are directly connected via an electrical connection to an external communication line 51, however it is also possible that the device comprises dataprocessing means for processing data from sensing means and/or for controlling actuators. Next to sensing means and/or actuators which are comprised in one or more microreactors, device sensing means and device actuators are comprised in the device 40. Such actuators, such as the heating and/or cooling which is provided in the heating and/or cooling zones 44 provide for example for a temperature conditioning for one or more microreactors or for a temperature conditioning in a temperature zone comprised in one or more microreactors. Further, the device 40 can comprise sensing means, such as temperature sensors, pressure sensors, etc. The actuators and/or sensing means comprised in the device 40 can for example be directly connected via an electrical connection to an external communication line 51, however it is also possible that the sensing means and/or actuators comprised in the device 40 are coupled to processing means for processing sensing means data from the device sensing means and/or for controlling the actuators in the device, i.e. the device actuators.

The upper part 41 and the lower part 42 can be connected to each other via a seal or any other means which is known per se, for achieving a gas-tight connection between the upper part 41 and the lower part 42. For controlling environmental conditions for reactions taken place in a microreactor positioned in the device, it is possible to supply a gas, such as an inert gas to a space which is enclosed by the device 40, and in which the microreactors are positioned. To accomplish this, the device 40 can comprise a surrounding gas supply port, via which an surrounding gas, such as an inert gas can be supplied to a space surrounding the one or more microreactors positioned in the device 40. Further, it is possible that the device 40 comprises microreactor identification means (not

shown) for identifying a type of microreactor which is positioned in the device. Thus, errors can be eliminated, as the microreactor identification means identify the type of microreactor which is positioned in the device.

5 Fig. 4 shows, in a partly transparent, schematical view, a microreactor 50 comprising a layered structure comprising a connection layer 51 for establishing electrical connections with the device, a reactor layer 52 (which is in this example built up from a reactor top layer 52a and a reactor bottom layer 52b between which
10 e.g. reactor channels have been formed), and an inlet / outlet layer 53 comprising inlet port 54 and outlet port 55. The connection layer comprises contact means, such as contact pins, symbolically indicated by 51a. The inlet port 54 and outlet port 55 are each connected to a respective compartment 54a and 55a for storing and buffering a flow
15 of a respective input substance and output substance. The inlet / outlet layer 53 can further comprise high pressure connections (not shown) for supplying a medium under a high pressure to the microreactor, such as a pressurised gas for a pressure driven pump and high voltage electrical connections, e.g. for powering an
20 electro-osmotic pump. The layers can be connected to one another by means of e.g. bonding, melting, or a glue, such as an epoxy resin.

Thus, according to the invention, it is possible to perform chemical reaction on a plurality of different microreactors as the device in which at least one of the microreactors is received
25 comprises a set of device communication means, which are each designed for communicating a specific quantity with a microreactor communication means comprised in a microreactor, when the microreactor is positioned in the device, while each microreactor comprises a subset of the microreactor communication means for
30 communication with a subset of the device communication means. Thus, the device provides for a standardized amount of device communication means which all have a standardized position with respect to a microreactor positioned in the device, and each device can make use of a subset of the device communication means, being the device
35 communication means which are required for the specific reaction which is to take place on the specific microreactor, and therefore the specific microreactor comprises a subset of the microreactor communication means, corresponding to the subset of the device

communication means. In this manner, it is possible to use the device, simultaneously or consecutively with a plurality of different microreactors. Further, as the same device can be used with the plurality of different microreactors, with all microreactors a same set of external communication means is used as the same device is used. Thus, external devices, such as liquid dosing robots, dataprocessing systems, control systems, gas supply systems, etc. which are used in conjunction with the device when preparing, performing and/or evaluating the at least one chemical reaction, only need to be programmed and/or configured once, as with all different microreactors, the same device is used, and thus the same of external communication means is used, further increasing interchangeability and flexibility.

The device and microreactors according to the invention will now be described on the basis of an example. A hydrogenation of nitrobenzene to anilin requires a solution of nitrobenzene together with a hydrogen gas to be brought into contact under a pressure with a catalyst. A microreactor for performing such reaction comprises a liquid inlet port for injecting nitrobenzene, and another liquid inlet port for injecting a solvent. Hydrogen is supplied by supplying a hydrogen, e.g. a hydrogen gas, to the microreactor. Alternatively it is possible to supply a liquid, such as a water, which liquid is electrochemically hydrolysed in the microreactor, to the microreactor. For finding optimum reaction conditions, a plurality of reactions can be performed on a plurality microreactors, positioned in the device simultaneously. The plurality of reactions each differ from each other by one or more parameters, such as a concentration of nitrobenzene, a type of solvent, a pressure, a reaction temperature and a reaction time. With the plurality of microreactors being positioned in the device simultaneously, it is possible to provide a single external input port for providing pure nitrobenzene to the device. Therefore, the device comprises a divider and valves (which are known as such in the art) for transporting the nitrobenzene to respective device communication means for providing the nitrobenzene to the microreactors. Further, with the valves, a flow of nitrobenzene to each of the microreactors can be controlled individually. The device comprises a plurality of external input ports which are used for inputting different solvents. From each

external input port, solvent is guided to a respective liquid outlet means for providing the solvent to a respective liquid inlet means comprised in a respective microreactor.

The device in which the microreactors are positioned, comprises
5 a device temperature controller, such as a temperature controlled heater for adjusting an overall temperature in the device. Further, a temperature can be individually controlled in each microreactor, or part thereof, by a thermoresistor, heatercoil, Peltier unit or other (micro) heater comprised in each microreactor and positioned in
10 proximity of a reactor channel in the microreactor. As the reaction is exotherm, and might be very exotherm depending on reaction parameters, a further temperature control might be required in one or more of the microreactors. For this purpose, a temperature sensor, (semiconductor) temperature readout means and electrical connection
15 means for transmitting a signal comprising temperature information from the microreactor to the device, is comprised in one or more of the microreactors. In this way, the temperature in these microreactors, or a part of these microreactors, can be accurately controlled by controlling a one or more of the heaters described
20 above making use of the signal comprising the temperature information. Further, as during the reaction hydrogen is consumed, pressure might drop. By incorporating a pressure sensor in one or more of the microreactors, possibly in combination with electronic pressure sensor readout means in the microreactor, a respective
25 signal comprising pressure information can be created and read-out via an electrical contact means comprised in the microreactor. A change in pressure observed can be used by an external data processing system (such as a computer) as a measure for monitoring reaction speed, however it is also possible that the data processing
30 system, or a data processing means comprised in the device, controls a pressure by, making use of the pressure information derived from the signal, controlling an actuator regulating gas pressure for the particular microreactor. Further, a reaction progress can be followed by measuring a conductivity of the solution in each microreactor. For
35 that purpose, a conductivity sensor can be installed in the microreactors and can be readout via a respective electrical contact means. As further pH of the solution will be altered by a change in aniline concentration, measuring pH of the solution by a pH sensor

installed in each microreactor provides an indication of a progress of the reaction. Therefore, a pH sensor is installed in each microreactor and read-out via an electrical contact means. Thus, the device comprises a set of device communication means, each device communication means for communicating a quantity, such as in this example liquid nitrobenzene, the solvent, electrical power for powering a device heater, a temperature signal, a pressure signal, a pressure regulating means, a signal comprising pH information, and possibly further device communication means not mentioned above. All microreactors comprise a subset of microreactor communication means for communicating a subset of the quantities required with the device communication means. Next to the reactions described, other reactions, making use of e.g. a different reaction mechanism or different substances, can be performed with the device, the other reactions making use of different microreactors, each having their own subset of device communication means for communicating one or more quantities with the device.

CLAIMS

1. A system for performing at least one chemical reaction on a plurality of different microreactors, the system comprising a device
5 having positioning means designed for at least temporarily receiving, at a fixed position within the device, of at least one of the plurality of different microreactors,

the device comprising a set of device communication means, each
10 device communication means being designed for communicating a specific quantity with the at least one microreactor at a specific location relative to the microreactor received in fixed position in the said device,

15 the system further comprising the plurality of microreactors, each one of the microreactors comprising a subset of microreactor communication means for communicating a subset of the said specific quantities with a corresponding subset of the device communication means, when the microreactor is received in fixed position in the
20 device,

wherein each particular microreactor communication means for communicating a particular specific quantity is positioned on an identical location relative to the device on each of the
25 microreactors comprising the particular microreactor communication means, when positioned in the device.

2. The system according to claim 1, characterised in that at least one of the device communication means and at least one of the
30 corresponding microreactor communication means comprised in at least one of the microreactors are designed for communicating a substance with the microreactor, when positioned in the device.

3. The system according to claim 2, characterised in that the device
35 communication means comprise a gas outlet means and in that the microreactor communication means comprise a gas inlet port.

4. The system according to claim 2 or 3, characterised in that the device communication means comprise a gas inlet means and in that the microreactor communication means comprise a gas outlet port.
- 5 5. The system according to any of claims 2 - 4, characterised in that the device communication means comprise a liquid outlet means and in that the microreactor communication means comprise a liquid inlet port.
- 10 6. The system according to any of claims 2 - 5, characterised in that the device communication means comprise a liquid inlet means and in that the microreactor communication means comprise a liquid outlet port.
- 15 7. The system according to any of the preceding claims, characterised in that at least one of the microreactors comprises a chip.
8. The system according to claim 7, characterised in that the chip
20 comprises an array of reaction wells, each reaction well for performing a chemical reaction.
9. The system according to claim 7 or 8, characterised in that the
25 chip comprises a flow path for guiding a flow of a substance in or on the chip.
10. The system according to any of the preceding claims, characterised in that at least one of the device communication means and at least one of the corresponding microreactor communication
30 means comprised in at least one of the microreactors are designed for establishing an electrical connection between the device and the microreactor, when positioned in the device.
11. The system according to claim 10, characterised in that the
35 device communication means comprise electrical connection means and in that the microreactor communication means comprise an electrical connection port.

12. The system according to claim 11, characterised in that at least one of the plurality of microreactors comprises sensing means for sensing a parameter on or in the microreactor, the sensing means being connected to at least one of the electrical connection ports.

5

13. The system according to claim 11 or 12, characterised in that at least one of the plurality of microreactors comprises an actuator which is connected to one of the electrical connection ports.

10 14. The system according to claim 12 or 13, characterised in that the sensing means comprise a temperature sensor.

15. The system according to claim 13 or 14, characterised in that the actuator comprises a microreactor temperature conditioner.

15

16. The system according to claim 15, characterised in that the microreactor temperature conditioner is designed for altering a temperature in a temperature zone of the microreactor.

20 17. The system according to any of claims 13 - 16, characterised in that the actuator comprises a pump.

18. The system according to claim 17, characterised in that the pump is an electro-osmotic pump.

25

19. The system according to any of claims 12 - 18, characterised in that the sensing means comprise a pressure sensor.

20. The system according to any of the preceding claims, characterised in that the device comprises device sensing means and/or device actuators which are positioned in a fixed position with regard to the device communication means.

30

21. The system according to claim 20, characterised in that the device actuators comprise pressure adaptation means for adapting a pressure in a pressure zone comprised in the device.

35

22. The system according to claim 20 or 21, characterised in that the device actuators comprise device temperature conditioning means for conditioning a temperature in a temperature zone comprised in the device.

5

23. The system according to any of the preceding claims, characterised in that the device further comprises data processing means for processing sensing means data and/or device sensing means data and/or for controlling actuators and/or device actuators.

10

24. The system according to claim 23, characterised in that the device further comprises a communication interface connected to the data processing means, for communication with a data processing device.

15

25. The system according to any of the preceding claims, characterised in that each of the plurality of microreactors comprises microreactor identification means for identifying the microreactors and in that the device comprises microreactor identification readout means for reading out an identification of a microreactor positioned in the device.

20

26. The system according to any of the preceding claims, characterised in that the device further comprises at least one external communication means for communicating at least one of the at least one quantities with an external device.

25

27. The system according to any of the preceding claims, characterised in that the device further comprises a housing for enclosing at least one microreactor when positioned in the device.

30

28. The system according to claim 27, characterised in that the housing comprises a plurality of compartments, each compartment for enclosing at least one microreactor when positioned in the device.

35

29. The system according to any of claims 7 - 28, characterised in that the microreactor comprises a layered structure comprising one or more layers chosen from a group of layers comprising at least one

electrical layer, at least one reactor layer and at least one inlet/outlet port layer.

30. A device for a system according to any of the preceding claims.

5

31. The device according to claim 30, holding a plurality of microreactors.

32. The device according to claim 30 or 31, comprising microreactor identification means for identifying a type of microreactor positioned in the device.

10

33. A microreactor for use in a system according to any of claims 1 - 29.

15

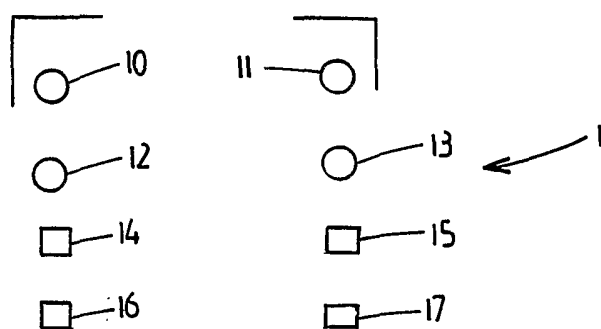


Fig. 1

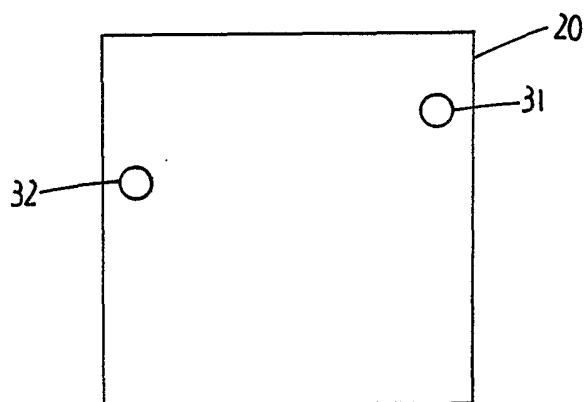


Fig. 2a

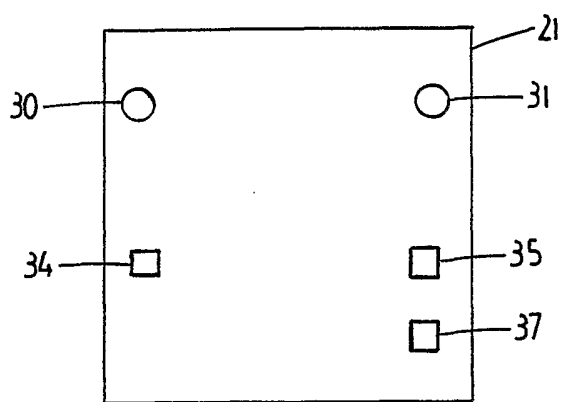


Fig. 2b



Fig. 2c

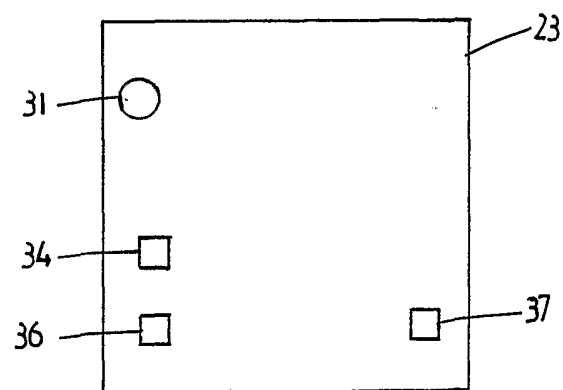


Fig. 2d

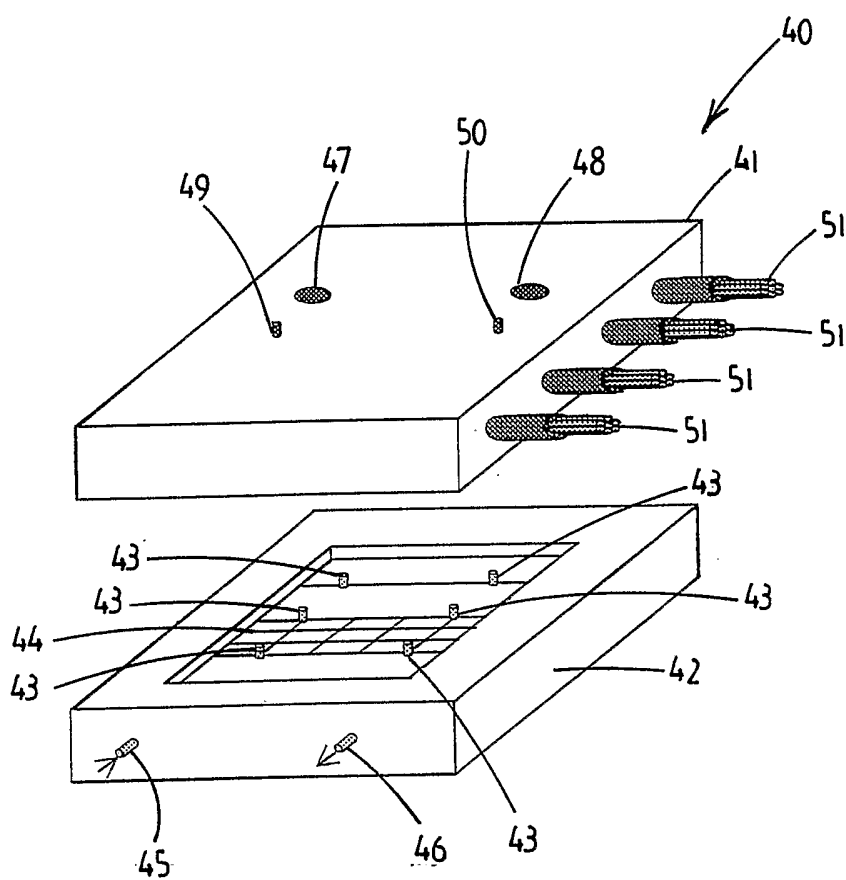


Fig. 3

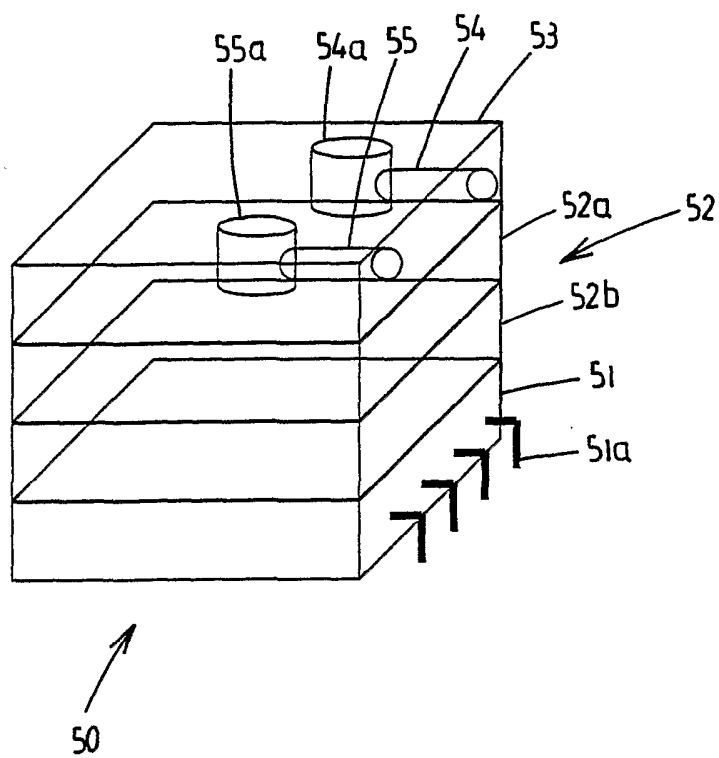


Fig. 4-

INTERNATIONAL SEARCH REPORT

International Application No

PCT/NL 02/00507

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 B01J19/00 B01L3/00

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)

IPC 7 B01J B01L

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	WO 00 62919 A (SCHWESINGER NORBERT ;HEIM ULF (DE)) 26 October 2000 (2000-10-26) abstract; claims 1-9; figure 1 ---	1-29
X	WO 00 78454 A (AGILENT TECHNOLOGIES INC ;CALIPER TECHN CORP (US)) 28 December 2000 (2000-12-28) abstract page 4, line 9 - line 30 page 8, line 1 -page 10, line 33 page 13, line 32 -page 14, line 20 ---	1-29
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international 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)
- *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

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 invention

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

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.

& document member of the same patent family

Date of the actual completion of the international search

3 April 2003

Date of mailing of the international search report

11/04/2003

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/NL 02/00507

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 89681 A (CELLULAR PROCESS CHEMISTRY INC) 29 November 2001 (2001-11-29) page 17, line 22 -page 20, line 30; figures 8-11 ---	1-29
X	DE 198 54 096 A (MERCK PATENT GMBH) 25 May 2000 (2000-05-25) the whole document ---	1-29
X	US 5 580 523 A (BARD ALLEN J) 3 December 1996 (1996-12-03) claim 1; figure 3 ---	1
E	DE 101 06 996 A (MERCK PATENT GMBH) 5 September 2002 (2002-09-05) the whole document -----	1

INTERNATIONAL SEARCH REPORT

international application No.
PCT/NL 02/00507

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 30-33
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:
see FURTHER INFORMATION sheet PCT/ISA/210
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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

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.:
4. ☐ 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

Continuation of Box I.2

Claims Nos.: 30-33

Present claims 30 and 33 relate to an extremely large number of possible devices. In fact, these claims contain so little technical features (apart from being suitable for use in a system as described in claim 1) that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Dependent claims 31 and 32 contain insufficient technical features defining the device to render them clear (and/or concise). Consequently, the search has been carried out for those parts of the application which do appear to be clear (and/or concise), namely claims 1-29.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/NL 02/00507

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