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(54) **Method and system of injecting.**

(57) The present disclosure relates to a method of injecting objects, such as eggs, with a fluid, wherein said objects each comprise at least two object parts, such embryo tissue, embryotic or allantoic fluid and an air pocket, of which at least one object part is to be injected, by advancing injection needles to a determined depth, which depth is expected to correspond with the at least one object part to be injected, into the objects and injecting fluid into the objects at the determined injection depth.

A corresponding injection system is disclosed.

Also, an independent calibration mechanism/algorithm is disclosed.

METHOD AND SYSTEM OF INJECTING

The present disclosure relates to a method and system of injecting fluid into or withdrawing fluid from a plurality of objects, such as eggs.

Merely by way of example, reference is made here to US-7165507, which teaches individual drive of a plurality of injection needles for injection of a plurality of eggs. According to this disclosure, pressure in or flow of fluid to flow through each needle is measured continuously as the needles move into the individual eggs. The needles are individually driven into individual eggs. Depending on a change in the measured pressure or flow, assuming that a desired location in or portion of the egg is reached, the position of which location or portion is beforehand not exactly known, the movement is stopped to perform injection or extraction. Thereby the individual movement of each of the plurality of needles for injecting fluid into or withdrawing fluid is halted to continue the injection into or extraction from in particular embryo's in the eggs.

This prior art teaching has several disadvantages. As an exemplary disadvantage, each needle must be equipped with an individual drive and control over the drive, wherein the drive and the control need to be responsive to measurements of pressure and/or flow in order to stop an advance of a needle in a particular egg at a desired location. As a consequence, the prior art system and method are costly, complex, and prone to malfunction. In particular, such a known system and method is likely to decide that the needle has advanced into an embryo, when the pressure increases and/or flow reduces. However, such an occurrence can be due to blockage of any particular needle.

Embodiments of the present disclosure aim at reducing or even obviating disadvantages of the prior art method and system. To this end a method is provided of injecting a objects, such as eggs, with a fluid, wherein said objects each comprise at least two object parts, such embryo tissue, embryotic or allantoic fluid and an air pocket, of which at least one object part is to be injected, the method comprising: advancing injection needles to a determined depth, which depth is expected to correspond with the at least one object part to be injected, into the objects and injecting fluid into the objects at the determined injection depth; monitoring pressure or flow of the fluid at least during injecting; and detecting an operational state of the needle and/or the fluid based on the monitored pressure or flow. Further, an injection system is provided, which is configured to inject objects, such as eggs, with a fluid, wherein said objects each comprise at least two object parts, such embryo tissue, embryotic or allantoic fluid and an air pocket, of which at least one object part is to be injected, the system comprising: a supply configured to provide a group of at least one object; needles connected with at least one drive configured for selective movement of the objects and the needles relative to one another, a control configured to inject needles into the objects to a determined injection depth for injection of the objects, which depth is set to correspond with the at

least one object part to be injected, and to advance the injection needles to the determined depth into the objects and injecting fluid into the objects at the determined injection depth; at least one sensor configured to monitor pressure or flow of the fluid at least during injecting, and to generate a monitoring signal sent to the control; and wherein the control is further configured to detect an operational state of the needles and/or the fluid based on the monitoring signal representing the monitored pressure or flow. It is noted that the method and system of the present disclosure entirely break with the prior art individual object based approach, to allow detection of air bubbles in fluid and/or partial or full blockage of needles and/or fluid lines. The benefits with respect to malfunction system detection are considered to outweigh any spurious misinjections, for example in another object part than an embryo, over the numerous insufficiently injected objects, which could occur in the prior art methods and systems, when needles are partially or fully blocked and the erroneous conclusion is drawn that injection has taken place in a desired object part.

The present disclosure comprises a number of preferred embodiments, some of which are represented in the below description under reference to the appended drawings, and/or defined in appended dependent claims.

For instance, the method may – in a specific embodiment – comprise that detecting the operational state of the needle and/or of the fluid comprises comparing a monitored pressure or flow with an operational reference. The control may be configured to detect the operational state of the needles and/or of the fluid by comparing a monitored pressure or flow with an operational reference. In such an embodiment the method may be such, that the operational reference comprises an expected pressure or flow change in time during and/or after injecting the objects, based on desired working conditions of the needle and/or connections thereto and in the fluid. In relation to the system it is noted that the operational reference may comprise an expected pressure or flow change in time during and/or after injecting the objects, based on desired working conditions of the needle and/or connections thereto and in the fluid.

In an alternative or additional embodiment, the method may be such that monitoring is maintained during a period after injecting the fluid. For the corresponding system, at least one of the sensor and the control is configured to continue monitoring during a period after injecting the fluid.

In an alternative or additional embodiment, the method may be such that determining the injection depth, which is expected to correspond with the at least one object part to be injected, comprises: providing a test group of at least one object; stepwise advancing an injection needle to at least two different depths in and injecting fluid at each of the two different depths into each of the at least one object of the test group; selecting one of the at least two different depths as the determined injection depth at which the object part to be injected is arranged in the at least one object of the test group based on an injection pressure or injection flow relative to an expected

injection pressure of injection flow at injection of the fluid at each of the at least two different depths; and injecting all of a plurality of objects other than the objects in the test group to the determined injection depth of the object part to be injected of the at least one object of the test group. In such an embodiment the method may be such that the expected injection pressure or injection flow comprises an object part reference of an expected pressure or flow change in time during and/or after injecting the objects, based on injecting the fluid in distinct ones of the object parts of the objects.

Correspondingly, the system may additionally or alternatively exhibit the features, that the injection depth, which is set to correspond with the at least one object part to be injected, is set through: the control being configured to advance needles into objects of a test group using the drive and to stepwise advance the injection needles to at least two different depths in and injecting fluid at each of the two different depths into each of the at least one object of the test group; wherein the control is further configured to select one of the at least two different injection depths as the determined injection depth at which the object part to be injected is arranged in the at least one object of the test group from a injection pressure or injection flow relative to an expected injection pressure of injection flow at injection of the fluid at each of the at least two different depths; and wherein the needles and drives are connected with the control and are together with the control configured to inject all of a plurality of objects other than the objects in the test group to the determined injection depth of the object part to be injected of the at least one object of the test group. In such an embodiment, the system may exhibit the further feature that the expected injection pressure or injection flow comprises an object part reference of an expected pressure or flow change in time during and/or after injecting the objects, based on injecting the fluid in distinct ones of the object parts of the objects. Especially if a highly accurately determined expected or desired injection depth is available, which is also a dependent subject of the present disclosure, the risk of erroneous injection in another object part than a desired object part can effectively be prevented from occurring.

With the method and injection system exhibiting these assemblies of features, disadvantages of prior art methods and systems can be reduced, if not overcome. In fact, the embodiments of the present disclosure rely on obtaining predetermined injection depth information from a test group of objects, in particular eggs, in a so-called calibration step, to thereafter inject needles into the subsequent larger populations of objects, eggs, all to the same injection depth, without individual measurement and the like. Once the calibration is performed, based on the test group, all of the objects that need to be injected are injected simultaneously, possibly in groups of simultaneously injected objects, and possibly using test groups repeatedly and/or intermittently, and to the same depth. This approach based on identical treatment with respect to injection depths of all of the objects to be injected after the test group, is completely opposite and consequently

novel and inventive, relative to the prior art method and system that are entirely dedicated to individual injection and measurement. It is acknowledged here that the approach to injection according to the present disclosure may result in sporadic mis-injection, for example if in an individual egg the embryo is at an entirely different location than all the embryos of the eggs in the test group, which is however entirely and more than compensated for by the fact that the embodiments of the present disclosure allow detection of blockage in individual needles in every degree, as well as the presence of air bubbles in injection fluid, and the like. Tests have surprisingly shown that the common approach to the task of injection into great numbers of individual objects with the ability to detect any degree of blockage and the presence of air bubbles far outweighs any capability according to the prior art of individual injection per separate object to a injection depth, that is beforehand not known.

In a specific embodiment of the present disclosure related to a method, the test group comprises two or more objects, and the step of determining the injection depth comprises determining the injection depth for most certain injection of the fluid into the object part to be injected for each or most of the two or more objects in the test group. In a specific embodiment of the present disclosure related to a system, the test group comprises two or more objects, and the control is configured to determine the injection depth by determining the injection depth for most certain injection of the fluid into the object part to be injected for each or most of the two or more objects in the test group. By increasing the test group and the number of objects therein, a higher degree of accuracy can be attained. For each of the objects in the test group, a necessary injection depth can be determined, for instance stepwise, by advancing an injection needle per object in the test group over a predetermined distance into the object, stopping advance of the needle, and performing a test injection or extraction at the reached injection depth. Depending on the instantaneous pressure or flow - and therefore not on the basis of any continuous change in any one or more than one of these parameters of pressure and/or flow - embodiments of the method and/or system can decide on the nature of the object part, into which the injection needle at the reached injection depth extends.

In a specific embodiment of the present disclosure related to a method, the step of determining the injection depth comprises distinguishing between injecting fluid into air, into fluid and into tissue based on the object part reference, and setting a depth at a one of the at least two different injection depths, at which the injection pressure or injection flow most closely approximates the object part reference corresponding with the object part to be injected, as the determined injection depth. In a specific embodiment of the present disclosure related to a system, the control is configured to determine the injection depth by distinguishing between injecting fluid into air, into fluid and into tissue based on the object part reference, and setting a depth at a one of the at least two different injection depths, at which the injection pressure or injection flow most

closely approximates the object part reference corresponding with the object part to be injected, as the determined injection depth.. Thus the secure manner of distinguishing is provided between injection into the air pocket, a fluid in the egg or into the embryo.

A specific embodiment of the present disclosure related to a method, further comprises: monitoring the injection pressure or injection flow for each individual injection needle during injection of fluid simultaneously in a plurality of objects. In a specific embodiment of the present disclosure related to a system further comprising a plurality of pressure or flow sensors, wherein the control is configured to monitor the injection pressure or injection flow for each individual injection needle during injection of fluid simultaneously in a plurality of objects. These features relate to the situation after having set or determined a preferred or necessary injection depth, after which all of the objects or eggs to be injected will be injected to the same injection depth. In such an embodiment, the method may further comprise: deciding that an injection needle is at least partially blocked, if at or after injection of fluid into the objects, the injection pressure or flow drops slower than the expected for the object part to be injected. The method may further comprise at least one of replacing, unblocking or cleaning the injection needle, when a difference between a monitored pressure or flow drop and an expected pressure or flow drop or between a monitored pressure or flow drop and the operational reference corresponding with the object part to be injected exceeds a predetermined threshold. The system may further indicate at least one of replacing, unblocking or cleaning the injection needle, when a difference between a monitored pressure or flow drop and an expected pressure or flow drop or between a monitored pressure or flow drop and the operational reference corresponding with the object part to be injected exceeds a predetermined threshold. The control may further be configured to decide that an injection needle is at least partially blocked, if at or after injection of fluid into each of the plurality of objects other than the objects in the test group the injection pressure or flow drops slower than the reference corresponding with the object part to be injected, and optionally at least one of replacing, unblocking or cleaning the injection needle, when a difference between a monitored pressure or flow drop and the reference corresponding with the object part to be injected exceeds a predetermined threshold. In such an embodiment of the present invention it is even possible to continue to apply a partially blocked needle, for instance if the degree of blockage is sufficient to ensure that adequate amounts of fluid are injected or extracted. In yet a further refined form of this embodiment the method further comprises: administering an additional fluid injection and monitoring the injection pressure or injection flow for an injection needle suspected of blockage, before deciding that the injection needle is blocked, if again thereafter injection pressure or flow drops slower than an expectation or the operational reference corresponding with the object part to be injected. With respect to the system the control may be further configured to administer an additional fluid injection and monitor the injection pressure or injection flow for an injection

needle suspected of blockage, before deciding that the injection needle is blocked, if again thereafter injection pressure or flow drops slower than an expectation or the operational reference corresponding with the object part to be injected.

In an embodiment at least based on monitoring, the method may further comprise: deciding that an object is absent, if at injection of fluid into the objects, the injection pressure or flow reduces more quickly than an expectation or the operational reference corresponding with the object part to be injected.

In an embodiment at least based on monitoring, the method may further comprise: deciding on air bubble presence in the injection fluid, if at injection of fluid into the objects, the injection pressure or flow reaches a lower maximum than expected or than the operational reference corresponding with the object part to be injected.

In an embodiment of the system, the controller may be configured to decide: that an object is absent, if at injection of fluid into the objects, the injection pressure or flow reduces more quickly than an expectation or operational reference corresponding with the object part to be injected, and/or on air bubble presence in the injection fluid, if at injection of fluid into the objects, the injection pressure or flow reaches a lower maximum than expected or than the operational reference corresponding with the object part to be injected.

Herein below, specific embodiments are described, referring to the appended drawing, in which the same or similar reference numbers can be employed for the same or similar elements, components and/or aspects. The embodiments in the appended drawing are by no means to be interpreted as limiting on the scope of protection for embodiments of the present disclosure, as defined in the appended claims. In the appended drawing:

figure 1 exhibits a first embodiment of a system according to the present disclosure, in which simultaneously the method according to the present disclosure is embodied;

figure 2 exhibits a second embodiment of a system according to the present disclosure, in which simultaneously the method according to the present disclosure is embodied;

figures 3 – 6 exhibit changes in time of pressure in a fluid injected into an object, wherein specific detectable circumstances play a role; and

figures 7 and 8 exhibit a curve of pressure over time to clarify detection of specific circumstances.

Figure 1 shows a system 1 according to the present disclosure, wherein the fluid supply 2 in the form of for example of vessel is provided in conjunction with a pump 3. In the exhibited embodiment, the exemplary field of application is injection of eggs.

When referring in the present disclosure to injection, reference is made to injection of the needle, regardless of an intended purpose of injecting fluid into or extracting fluid out of the

objects and the eggs more in particular. The fluid supply 2 can be a receptacle to receive fluids extracted from individual eggs 4.

A fluid line 5 is connected to pump 3, and branches out into to individual needles 6 via non-return valves 7 and flexible line parts 8. Between the non-return valves 7 and the flexible line parts 8, pressure sensors 9 are provided. Pressure sensors 9 are connected with the control 10 to provide pressure measurement results to the control 10. Pressure sensors nine can be replaced by flow sensors (not shown).

Each of the needles 6 is, in the embodiment of figure 1, provided with an individual drive 11, comprising a motor 12 and a toothed wheel 13 acting on a rack 14, to control movement of each of the needles 6 in the direction of double arrow A. Alternatively, eggs 4 can be arranged on supports 15, to move up or down there with, to and from needles 6, using alternative or additional drives 16. Motors 12 or drives 16 will be driven by control 10. Alternatively, as shown in figure 2, the individual motors 12 can be replaced by a common motor 12 in an alternative embodiment of the system 17. The common motor 12 in the embodiment of figure 2 can be connected with the toothed wheels 13 via an axis 18. Likewise, individual drives 16 can be replaced by a single or common drive 16 in the embodiment of figure 2, to raise or lower supports 15 under eggs 4 synchronously. The embodiment according to figure 1 may have a slight preference over the embodiment of figure 2, as any injection needle 6 can be restrained from reaching a deeper injection depth than necessary, also for the eggs 4 in the test group, in particular if the same configuration is employed both for calibration and for subsequent injections. In the embodiment according to figure 2, all injection needles 6 will be driven during calibration to a predetermined number of penetration depths, regardless of whether or not already an embryo was encountered at a lower injection depth. On the other hand, the configuration according to figure 2 allows for the same system to be used, during the calibration step and subsequent injection steps for injecting high numbers of eggs simultaneously or in sequence. However, the system according to figure 1 can also be employed both during calibration and subsequent injection of large numbers of eggs other than the eggs 4 in the test group, simply by driving the motors 12 in synchronicity.

In a test or calibration phase, control 10 will drive motors 12 or drives 16 in such a way, that the needles 6 advance into eggs 4 in a stepwise manner to a first depth at D1, a second depth at D2, a third step at D3, etc. At reaching each of the predetermined depths, relative movement of the eggs 4 in relation to needles 6 is paused for a test injection or extraction. Based on values measured with sensors 9, it is determined for each of the eggs for at each of the depths D1, D2,…, what matter was encountered; air pocket, fluid, or embryo. Based on a non-limiting assumption that injection into embryos is desired, and of the test population of eggs 4 in the test or calibration phase, the highest probability of encountering an embryo is determined at injection depth D2 from the depths of D1, D2, …, the decision can be taken to thereafter inject all eggs other than the eggs

4 of the test group to this determined injection depth D2 and achieve the highest degree of certainty that embryos will be injected as a consequence. As a consequence, the prior art concept of individual injection to a beforehand unknown injection depth is relinquished, in favour of an algorithm or method where large numbers of eggs other then the eggs 4 of the test group will all be injected to the same injection depth, which will there before have been determined on the basis of results of measurements with respect to the eggs 4 in the test group. Alternatively, any other method to determine a desired or necessary injection depth having the highest possible degree of certainty about injection into a desired object part, may be employed to replace the described calibration. Further, the calibration as set out herein may be employed in combination with or for other purposes than subsequent injections, and may even form subject of an independent invention, even without any detection of an operational state of the system or any part or component thereof, or of the fluid.

Figure 3 exhibits a characteristic curve for injection into fluid, whereas figure 4 exhibits a similar characteristic curve for injection into tissue, for instance of an embryo. The characteristic curves referred to here exhibit pressure over time, wherein pressure can be measured using the pressure sensors 9 in figure 1 or 2. Similar or the same considerations would ensue, if pressure sensors 9 were replaced by flow sensors.

The maximum pressure value for injection into fluid 20 is only slightly less than a maximum pressure value for injection into tissue 21, which is self evident from or comparison of figures 3 and 4. Further, the curve for injection into fluid 20 falls away more sharply, after pressure from pump 3 is released, then the curve for injection into tissue 21. Consequently, from detection results at any given injection depth, without even movement of the injection needle relative to the object to be injected, it is possible to draw a conclusion about a location at which injection is taking place, and more in particular about an object part into which injection is taking place, for example in the test or calibration phase. It should be noted that for each of the curves in figures 3 – 8, the pump is deactivated at reaching a maximum pressure value or configured to maintain the maximum pressure value for a predetermined period of time, before deactivation. Conclusions about tissue or fluid, blockages of lines and/or needles, and about air bubbles in fluids to be injected can be drawn on the basis of measurements and curves, as will be explained herein below, in particular with respect to pressure build up and/or pressure release.

In figure 3 an additional curve 22 is depicted, which relates to the presence of air bubbles in the fluid to be injected. This is detectable from the consideration that a maximum value is considerably lower even than the maximum value of the curve for injection into fluid 21.

Figure 5 exhibits a curve 23, which can be detected on the basis of normal maximum pressure, but wherein there is no pressure drop after pressure from the pump 3 is released, to indicate blockage of a line or needle 6. If curve 23 is detected, pressure from pump 3 can be raised

further at 24, as depicted in figure 6. Thereby, confirmation of the suspected blockage can be obtained and/or an attempt can be directed at opening line or needle 6 on the basis of the pressure increase at 24.

Pressure in line 5 from pump 3 may exhibit at the needles 6 a curve shape 25 as in figure 7, based on intermittent injection of separate eggs, all to the same injection depth. Therein different phases can be distinguished, like entering the egg, applying pressure, maintaining pressure, releasing pressure, withdrawing needle from egg, supplying new egg, et cetera.

The enlarged representation of curve 25 in figure 8 clarifies that a number of aspects can be monitored in embodiments according to the present disclosure, for instance:

- bubbles were/are in line 5 or needle 6, at 26;
- line 5 and/or needle 6 is fully blocked at 27 or partially blocked at 28;
- injection is in tissue of for instance an embryo in an egg, at 25;
- injection is in fluid for instance in an egg surrounding the embryo at 29; and
- injection is in air, outside an egg or into the air pocket in the egg at 30; and
- a pump defect can be detected if no pressure is built up at all, which is not individually shown, but in such a case, the pressure will not rise from the horizontal axis.

It is noted that in case the injection is detected to be performed in outside air, in the fifth of the cases mentioned directly above, there is evidently no egg at the location of a particular needle. For instance, in figure 1 or 2, one of the eggs 4 may kept away from the path of movement of that needle, for example because the one of the eggs 4 does not contain any embryo or a dead embryo, which can have been detected in a detection step, wherein the egg may be kindled or otherwise examined. Subsequently, the support 15 can be held back from the needle 6, if the egg 4 is determined to be dead or missing an embryo, to avoid later contamination using the same needle 6 or superfluous injection in such an egg.

It should be noted that pump 3 can be deactivated during progress into the eggs in the test or calibration phase. The system does not monitor pressure of flow during movement for penetration of injection needle 6 into the egg. Pump 3 and monitoring are active only when the needle has advanced to one of a number of depths in the test or calibration phase, and are active in the subsequent operational phase only when the single determined injection depth is reached, and therefore also not during travel of the needle 6 to this depth, whereby a considerable amount of fluid to be injected can be saved. In particular if fluid to be injected is costly, such as medicines and/or antibiotics, this may result in a considerable benefit, in addition to the finding that it is possible to determine what object part is being injected from the profile of a pressure or flow curve.

After the above detailed description of particular embodiments of the present disclosure, it should be noted here that a scope of protection for these embodiments is however by no means to

be interpreted as limited to any specific feature, element, component or aspect, and that equivalent or alternative configurations may as well comply with the present disclosure and fall within the scope of protection therefore, as defined in the appended claims, unless such equivalent or alternative configurations fundamentally deviate from the requirements according to the appended claims. For instance, the method or system could rely on the creation of an injection table in the phase of calibration. Allowing for deviations in needles 6 and/or supports 15 can result in individual drive of each needle relative to a corresponding egg. Likewise, deviations in outer dimensions of individual eggs can also result in individual drive is for separate needles in their injection movement. A main consideration is that a constant injection depth is determined in the calibration phase and thereafter maintained, regardless of such needle or support variations or differences in outer dimensions of individual eggs, where in the injection phase subsequent to the calibration phase the presence of air bubbles and for partial blockages of fluid lines and more in particular injection needles can be detected. During calibration, the object part reference may be determined, where after in subsequent injections in a production phase detected pressure or flow may be set out against the operational reference that would indicate air bubbles or partial or full blockage, or the like.

The configurations in figures 1 and 2 are mainly described as relating to the calibration phase, but the same configurations are equally applicable in the subsequent injection phase, wherein large numbers of eggs are subsequently injected (which may include that fluid is to be extracted therefrom). Moreover, the calibration can be performed only once for all subsequent injections, and may be expected to yield a highly reliable object part reference about the desired or necessary injection depth. If a test group is sufficiently large, the resulting determined injection depth will be sufficiently accurate for all subsequent injections. Calibration may even be omitted entirely. From such examples it is abundantly clear that only the following claims impose limitations on the scope of protection for embodiments according to the present disclosure, to include equivalents and alternatives in as far as these are not excluded in or by the definitions according to the appended claims, and in particular the appended independent claims. Further, it is to be noted that the calibration described herein and defined in appended dependent claims 5 – 8 for calibration for determining a most preferred uniform injection depth for all needles during subsequent injections may be implemented independently from the steps and components for monitoring desired operation and the operational state of the system, and could be made subject of protection independent from such monitoring of the operational state of the system.

CONCLUSIES

1. Een werkwijze van injecteren van objecten, zoals eieren, met een vloeistof, waarbij de objecten elk ten minste twee object delen omvatten, zoals embryo weefsel, embriotische of allantoïsche vloeistof en een luchtzak, waarvan ten minste één object deel te injecteren is, welke werkwijze omvat:

- het inbrengen van injectienaalden tot een vooraf bepaalde diepte, welke diepte naar verwachting overeenkomt met het ten minste ene te injecteren object deel, in de objecten en het injecteren van de vloeistof in de objecten op de vooraf bepaalde diepte;
- het waarnemen van druk of stroming van de vloeistof ten minste gedurende het injecteren; en
- het detecteren van een operationele toestand van het systeem en in het bijzonder de naald en / of de vloeistof op basis van de waargenomen druk of stroming.

2. De werkwijze volgens conclusie 1, waarbij het detecteren van de operationele toestand van de naald en / of van de vloeistof omvat: het vergelijken van een waargenomen druk of stroming met een operationele referentie.

3. De werkwijze volgens conclusie 2, waarbij de operationele referentie omvat: een verwachte verandering in druk of stroming in de tijd, gedurende en / of na het injecteren van de objecten, op basis van gewenste werkzame omstandigheden van de naald en / of van de verbindingen daar naartoe en in de vloeistof.

4. De werkwijze volgens conclusie 1, 2 of 3, waarbij het waarnemen wordt voortgezet gedurende een periode na het injecteren van de vloeistof.

5. De werkwijze volgens een willekeurige van de voorgaande conclusies, waarbij het bepalen van de injectiediepte, welk naar verwachting overeenkomt met het ten minste ene te injecteren object deel, vooraf gaat aan de step van seriematige injectie, en omvat:

- het verschaffen van een test groep van ten minste één object;
- het stapsgewijs inbrengen van een injectienaald tot ten minste twee verschillende dieptes in en het injecteren van vloeistof bij elke van de twee verschillende dieptes in elke van het ten minste ene object van de test groep;
- het selecteren van één van de ten minste twee dieptes as de bepaalde injectie diepte waar het te injecteren object deel is gelegen in het ten minste ene object van de test groep op basis van een injectiedruk of injectiestroming, ten opzichte van een verwachte injectiedruk of injectiestroming bij injectie van de vloeistof bij elke van de ten minste twee verschillende dieptes; en
- het injecteren van alle van een aantal objecten, anders dan de objecten in de test groep, tot op de bepaalde injectie diepte van het te injecteren object deel van het ten minste ene object van de test groep.

6. De werkwijze volgens conclusie 5, waarbij de verwachte injectiedruk of injectiestroming een referentie omvat van een object deel van een verwachte verandering in druk of stroming in de tijd, gedurende and / of na het injecteren van de objecten, op basis van injectie van de vloeistof in afzonderlijke delen van de object delen van de objecten.

7. De werkwijze volgens conclusie 5 of 6, waarbij de test groep twee of meer objecten omvat, en de stap van het bepalen van de injectiediepte omvat: het bepalen van de injectiediepte voor een het meest zekere injectie van de vloeistof in het te injecteren object deel voor elke of de meeste van de twee of meer objecten in de test groep.

8. De werkwijze volgens conclusie 5, 6 of 7, waarbij de stap van het bepalen van de injectiediepte omvat: het onderscheiden tussen injectie van vloeistof in lucht, in vloeistof en in weefsel, op basis van de referentie van het object deel, en het instellen van een diepte bij een enkele van de ten minste twee verschillende injectiedieptes, waar de injectiedruk of stroming het dichtst de objectdeel referentie benadert, in overeenstemming met het te injecteren object deel, als de bepaalde injectiediepte.

9. De werkwijze volgens een willekeurige of meer dan één van de voorgaande conclusies, verder omvattende: het waarnemen van de injectiedruk en / of d injectiestroming voor elke afzonderlijke naald gedurende injectie van vloeistof gelijktijdig in een aantal objecten.

10. De werkwijze volgens een willekeurige of meer dan één van de voorgaande conclusies, verder omvattende: het besluiten dat een injectienaald ten minste gedeeltelijk is geblokkeerd, als tijdens of na injectie van vloeistof in de objecten de injectiedruk of injectiestroming trager daalt dan verwacht voor het te injecteren object.

11. De werkwijze volgens conclusie 10, verder omvattende: ten minste één van het vervangen, deblokkeren of reinigen van de injectienaald, wanneer een verschil tussen een waargenomen drukval of stromingsafname en een verwachte drukval of stromingsafname of een verschil tussen een waargenomen drukval of stromingsafname en de operationele referentie, die overeenkomt met het te injecteren object deel, een vooraf bepaalde drempel overschrijdt.

12. De werkwijze volgens conclusie 10 of 11, verder omvattende: het toedienen van een aanvullende vloeistofinjectie en het waarnemen van de injectiedruk of injectiestroming voo een injectienaald, van welke blokkering is vermoed, vaarafgaand aan het beslissen dat de injectienaald geblokkeerd is, indien daarna wederom de injectie drukval of injectie stromingsafname langzamer daalt dan een verwachting of dan de operationele referentie, die overeenkomt met het te injecteren object deel.

13. De werkwijze volgens conclusie 9, 10, 11, of 12, verder omvattende: het besluiten dat een object ontbreekt, indien tijdens injectie van vloeistof in de objecten, de injectiedruk of de injectiestroming sneller afneemt dan een verwachting of dan de operationele referentie die overeenkomt met het te injecteren object deel.

14. De werkwijze volgens een willekeurige van conclusies 9 – 13, verder omvattende: het besluiten dat een luchtbel aanwezig was in de injectievloeistof, indien bij injectie van de vloveistof in de objecten, de injectiedruk of injectiestroming een lagere maximale waarde bereikt dan verwacht of dan de operationele referentie die overeenkomt met het te injecteren object deel.

15. Een system dat is geconfigureerd om objecten, zoals eieren, met een vloeistof te injecteren, waarbij de objecten elk ten minste twee object delen omvatten, zoals embryo weefsel, embriotische of allantoïsche vloeistof en een luchtzak, waarvan ten minste één object deel te injecteren is, welke systeem omvat:

- een toevoer, welke is geconfigureerd voor het verschaffen van ten minste één object;
- naalden, welke zijn verbonden met ten minste één aandrijving welke is geconfigureerd voor selectieve beweging van de objecten en de naalden ten opzichte van elkaar;
- een besturing welke is geconfigureerd voor het injecteren van naalden in de objecten tot op een gewenste injectiediepte voor de objecten, welke diepte is ingesteld om overeen te komen met het ten minste ene te injecteren object deel, en om de injectienaalden voort te bewegen naar de bepaalde diepte in de objecten en het injecteren van de vloeistof in de objecten op de vooraf bepaalde diepte;
- ten minste één sensor, welke is geconfigureerd om de druk of de stroming waar te nemen, ten minste gedurende het injecteren, en om een waarnemingssignaal te genereren en naar de besturing te sturen; en
- waarbij de besturing verder is geconfigureerd om een operationele toestand van de naalden en / of de vloeistof waar te nemen op basis van het waarnemingssignaal dat de waargenomen druk of stroming representeert.

16. Het systeem volgens conclusie 15, waarbij de besturing is geconfigureerd voor het detecteren van de operationele toestand van de naald en / of van de vloeistof door het vergelijken van een waargenomen druk of stroming met een operationele referentie.

17. Het systeem volgens conclusie 16, waarbij de operationele referentie omvat: een verwachte verandering in druk of stroming in de tijd, gedurende en / of na het injecteren van de objecten, op basis van gewenste werkzame omstandigheden van de naald en / of van de verbindingen daar naartoe en in de vloeistof

18. Het systeem volgens conclusie 15, 16 of 17, waarbij ten minste één van de sensor en de besturing is geconfigureerd voor het verder gaand waarnemen in een periode na het injecteren van de vloeistof.

19. Het systeem volgens een willekeurige van de voorgaande conclusies 15 – 18, waarbij het instellen van de injectiediepte, welk is ingesteld om overeen te komen met het ten minste ene te injecteren object deel, is ingesteld doordat:

- de besturing is geconfigureerd voor het inbrengen van injectienaalden in objecten van een test groep door gebruik te maken van de aandrijving en om de injectienaalden stapsgewijs in te brengen tot ten minste twee verschillende dieptes en het injecteren van vloeistof op elke van de ten minste twee verschillende dieptes in elke van het ten minste ene object van de test groep;
- waarbij de besturing verder is geconfigureerd voor het selecteren van één van de ten minste twee verschillende injectiedieptes als de bepaalde injectie diepte waar het te injecteren object deel is gelegen in het ten minste ene object van de test groep op basis van een injectiedruk of injectiestroming, ten opzichte van een verwachte injectiedruk of injectiestroming bij injectie van de vloeistof bij elke van de ten minste twee verschillende dieptes; en
- waarbij de naalden en de aandrijvingen zijn verbonden met de besturing en tezamen met de besturing zijn geconfigureerd om alle van een aantal objecten, anders dan de objecten in de test groep, te injecteren tot op de bepaalde injectie diepte van het te injecteren object deel van het ten minste ene object van de test groep.

20. Het systeem volgens conclusie 19, waarbij de verwachte injectiedruk of injectiestroming een referentie omvat van een object deel van een verwachte verandering in druk of stroming in de tijd, gedurende and / of na het injecteren van de objecten, op basis van injectie van de vloeistof in afzonderlijke delen van de object delen van de objecten.

21. Het systeem volgens conclusie 19 of 20, waarbij de test groep twee of meer objecten omvat, en de besturing is geconfigureerd voor het bepalen van de injectiediepte door het bepalen van de injectiediepte voor een het meest zekere injectie van de vloeistof in het te injecteren object deel voor elke of de meeste van de twee of meer objecten in de test groep.

22. Het systeem volgens conclusie 20 of 21, waarbij de besturing is geconfigureerd voor het bepalen van de injectiediepte door het onderscheiden tussen injectie van vloeistof in lucht, in vloeistof en in weefsel, op basis van de referentie van het object deel, en het instellen van een diepte bij een enkele van de ten minste twee verschillende injectiedieptes, waar de injectiedruk of stroming het dichtst de objectdeel referentie benadert, in overeenstemming met het te injecteren object deel, als de bepaalde injectiediepte

23. Het systeem volgens conclusie 19, 20, 21 of 22, verder omvattende een aantal druk- of stromingsmeters, waarbij de besturing is geconfigureerd voor het waarnemen van de injectiedruk en / of de injectiestroming voor elke afzonderlijke naald gedurende injectie van vloeistof gelijktijdig in een aantal objecten.

24. Het systeem volgens conclusie 23, waarbij de besturing verder is geconfigureerd voor het besluiten dat een injectienaald ten minste gedeeltelijk is geblokkeerd, als tijdens of na injectie van vloeistof in de objecten de injectiedruk of injectiestroming trager daalt dan verwacht voor het te injecteren object, een het aangeven van ten minste één van het vervangen, deblokkeren of reinigen van de injectienaald, wanneer een verschil tussen een waargenomen drukval of

stromingsafname en een verwachte drukval of stromingsafname of een verschil tussen een waargenomen drukval of stromingsafname en de operationele referentie, die overeenkomt met het te injecteren object deel, een vooraf bepaalde drempel overschrijdt

25. Het systeem volgens conclusie 24, waarbij de besturing verder is geconfigureerd voor het toedienen van een aanvullende vloeistofinjectie en het waarnemen van de injectiedruk of injectiestroming voor een injectienaald, van welke blokkering is vermoed, vaarafgaand aan het beslissen dat de injectienaald geblokkeerd is, indien daarna wederom de injectie drukval of injectie stromingsafname langzamer daalt dan een verwachting of dan de operationele referentie, die overeenkomt met het te injecteren object deel.

26. Het systeem volgens conclusie 23, 24, of 25, waarbij de besturing is geconfigureerd om te beslissen:

- dat een object ontbreekt, indien tijdens injectie van vloeistof in de objecten, de injectiedruk of de injectiestroming sneller afneemt dan een verwachting of dan de operationele referentie die overeenkomt met het te injecteren object deel, en / of
- dat een luchtbel aanwezig was in de injectievloeistof, indien bij injectie van de vloeistof in de objecten, de injectiedruk of injectiestroming een lagere maximale waarde bereikt dan verwacht of dan de operationele referentie die overeenkomt met het te injecteren object deel.

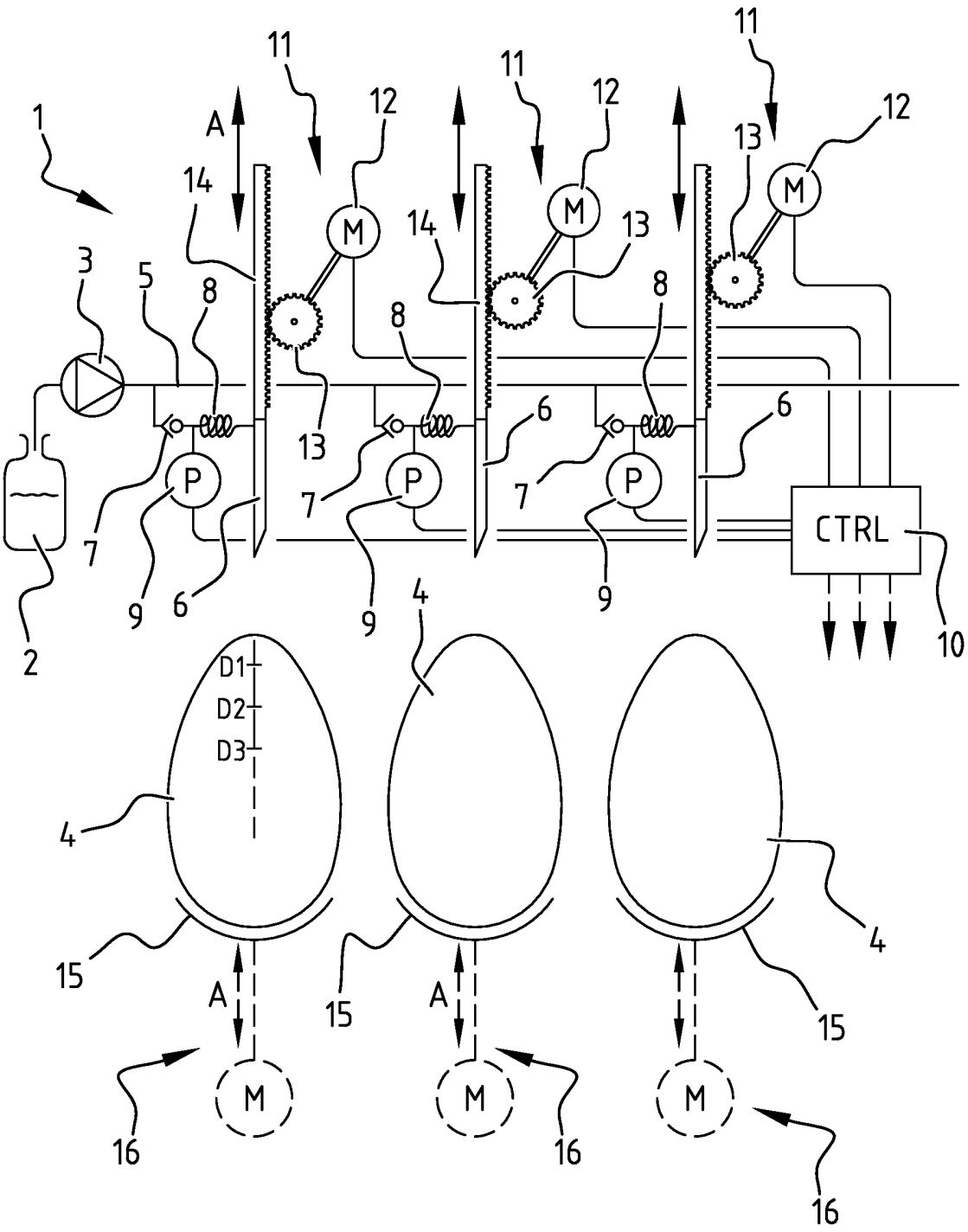
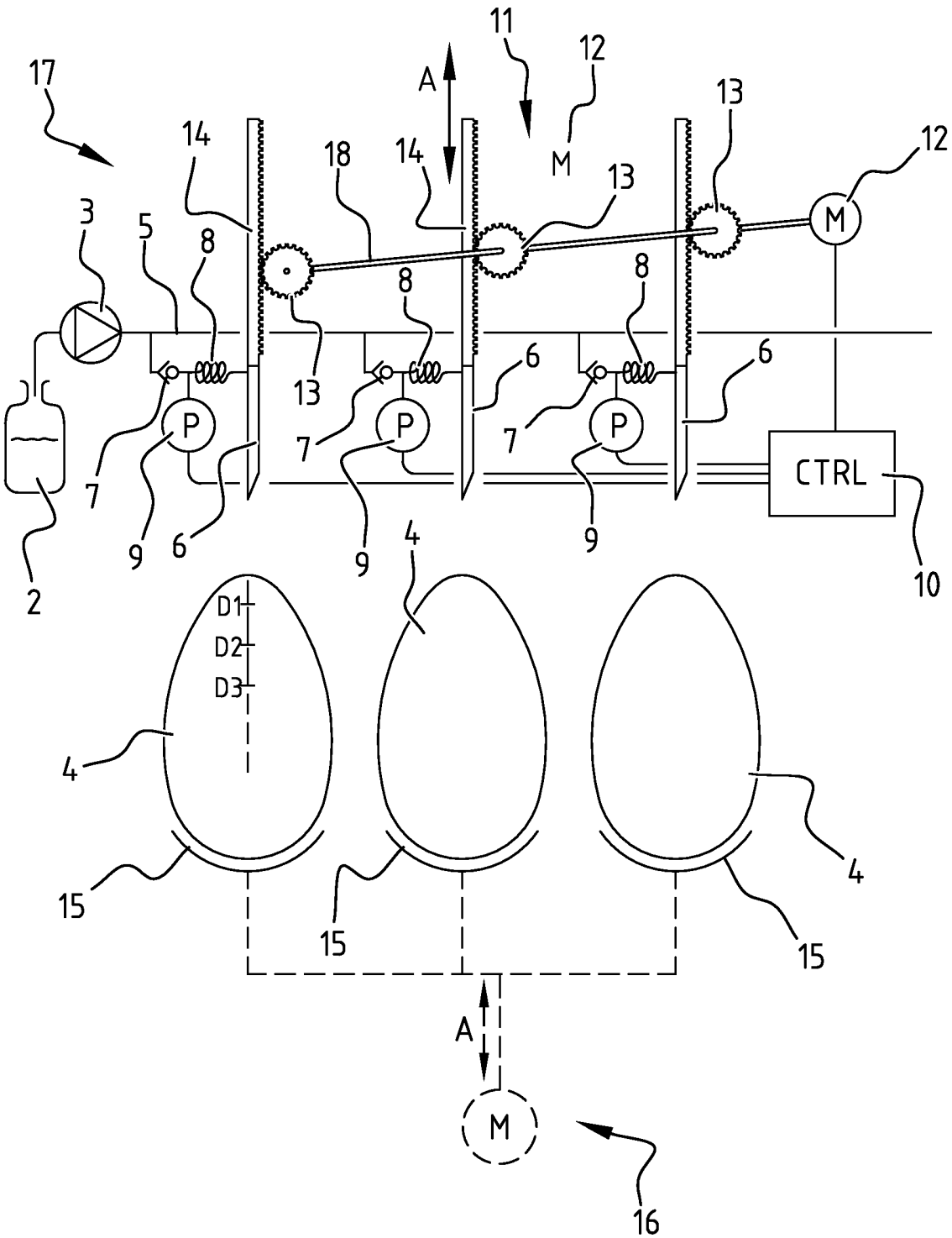


FIG. 1


17
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M
16

FIG. 2

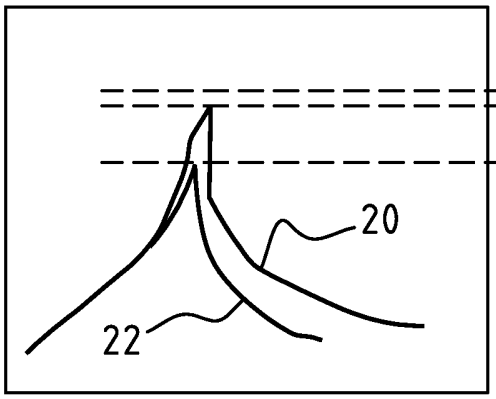

FIG. 3

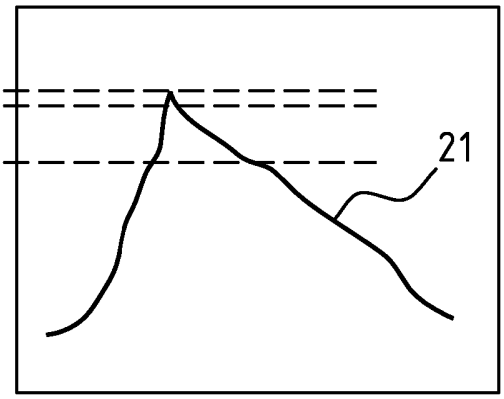

FIG. 4

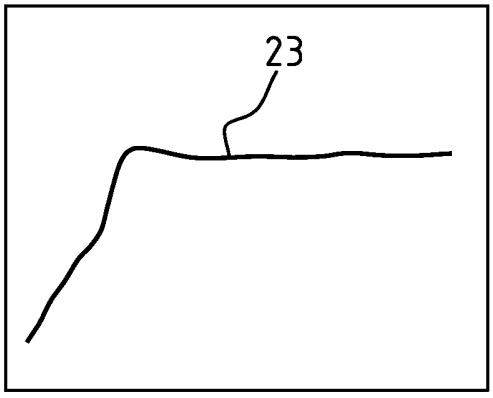

FIG. 5

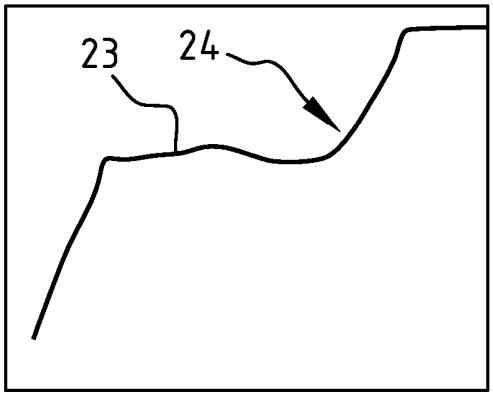

FIG. 6

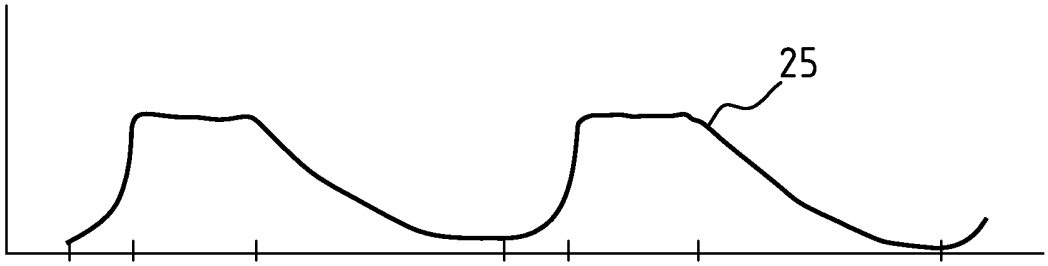

FIG. 7

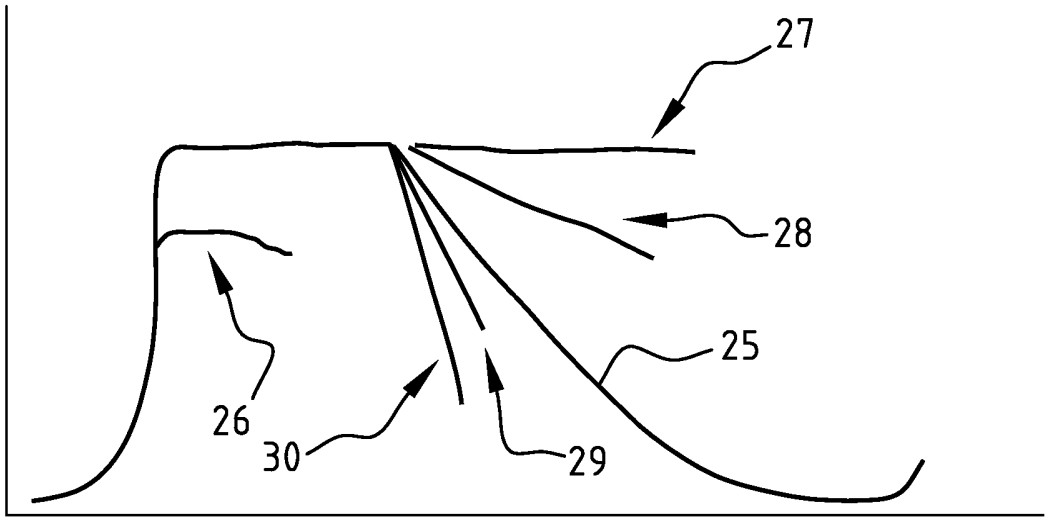

FIG. 8

ABSTRACT

TITLE: METHOD AND SYSTEM OF INJECTING

The present disclosure relates to a method of injecting objects, such as eggs, with a fluid, wherein said objects each comprise at least two object parts, such embryo tissue, embryotic or allantoic fluid and an air pocket, of which at least one object part is to be injected, by advancing injection needles to a determined depth, which depth is expected to correspond with the at least one object part to be injected, into the objects and injecting fluid into the objects at the determined injection depth.

A corresponding injection system is disclosed.

Also, an independent calibration mechanism/algorithm is disclosed.

SAMENWERKINGSVERDRAG (PCT)

RAPPORT BETREFFENDE NIEUWHEIDSONDERZOEK VAN INTERNATIONAAL TYPE

IDENTIFICATIE VAN DE NATIONALE AANVRAGE	KENMERK VAN DE AANVRAGER OF VAN DE GEMACHTIGDE
	W/2OY52/ML/15
Nederlands aanvraag nr. **2013433**	Indieningsdatum **08-09-2014**
	Ingeroepen voorrangsdatum
Aanvrager (Naam) **Viscon B.V.**	
Datum van het verzoek voor een onderzoek van internationaal type **06-12-2014**	Door de Instantie voor Internationaal Onderzoek aan het verzoek voor een onderzoek van internationaal type toegekend nr. **SN63142**

I. CLASSIFICATIE VAN HET ONDERWERP (bij toepassing van verschillende classificaties, alle classificatiesymbolen opgeven)

Volgens de internationale classificatie (IPC)

A01K45/00

II. ONDERZOCHTE GEBIEDEN VAN DE TECHNIEK

Onderzochte minimumdocumentatie

Classificatiesysteem	Classificatiesymbolen
IPC	**A01K**

Onderzochte andere documentatie dan de minimum documentatie, voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen

III. [X] **GEEN ONDERZOEK MOGELIJK VOOR BEPAALDE CONCLUSIES** (opmerkingen op aanvullingsblad)

IV. [ ] **GEBREK AAN EENHEID VAN UITVINDING** (opmerkingen op aanvullingsblad)

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

Nummer van het verzoek om een onderzoek naar de stand van de techniek
NL 2013433

A. CLASSIFICATIE VAN HET ONDERWERP
INV. A01K45/00
ADD.

Volgens de Internationale Classificatie van octrooien (IPC) of zowel volgens de nationale classificatie als volgens de IPC.

B. ONDERZOCHTE GEBIEDEN VAN DE TECHNIEK

Onderzochte miminum documentatie (classificatie gevolgd door classificatiesymbolen)
A01K

Onderzochte andere documentatie dan de mimimum documentatie, voor dergelijke documenten, voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen

Tijdens het onderzoek geraadpleegde elektronische gegevensbestanden (naam van de gegevensbestanden en, waar uitvoerbaar, gebruikte trefwoorden)
EPO-Internal, WPI Data

C. VAN BELANG GEACHTE DOCUMENTEN

Categorie °	Geciteerde documenten, eventueel met aanduiding van speciaal van belang zijnde passages	Van belang voor conclusie nr.
	ONVOLLEDIG ONDERZOEK zie aanvullingsblad C -----	
X,D	US 7 165 507 B2 (WOLFE STEPHEN P [US] ET AL) 23 januari 2007 (2007-01-23) in de aanvraag genoemd	15-18
A	* kolom 1, regel 32 - regel 59 * * kolom 4, regel 53 - kolom 5, regel 23 * * kolom 5, regel 65 - kolom 6, regel 3 * * kolom 6, regel 51 - kolom 7, regel 6 * * kolom 7, regel 52 - regel 59; figuren 1-5 *	19-26

	-/--	

[X] Verdere documenten worden vermeld in het vervolg van vak C.

[X] Leden van dezelfde octrooifamilie zijn vermeld in een bijlage

° Speciale categorieën van aangehaalde documenten

"A" niet tot de categorie X of Y behorende literatuur die de stand van de techniek beschrijft

"D" in de octrooiaanvrage vermeld

"E" eerdere octrooi(aanvrage), gepubliceerd op of na de indieningsdatum, waarin dezelfde uitvinding wordt beschreven

"L" om andere redenen vermelde literatuur

"O" niet-schriftelijke stand van de techniek

"P" tussen de voorrangsdatum en de indieningsdatum gepubliceerde literatuur

"T" na de indieningsdatum of de voorrangsdatum gepubliceerde literatuur die niet bezwarend is voor de octrooiaanvrage, maar wordt vermeld ter verheldering van de theorie of het principe dat ten grondslag ligt aan de uitvinding

"X" de conclusie wordt als niet nieuw of niet inventief beschouwd ten opzichte van deze literatuur

"Y" de conclusie wordt als niet inventief beschouwd ten opzichte van de combinatie van deze literatuur met andere geciteerde literatuur van dezelfde categorie, waarbij de combinatie voor de vakman voor de hand liggend wordt geacht

"&" lid van dezelfde octrooifamilie of overeenkomstige octrooipublicatie

Datum waarop het onderzoek naar de stand van de techniek van internationaal type werd voltooid	Verzenddatum van het rapport van het onderzoek naar de stand van de techniek van internationaal type
21 april 2015	

Naam en adres van de instantie	De bevoegde ambtenaar
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Postma, Rob

1

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

Nummer van het verzoek om een onderzoek naar de stand van de techniek
NL 2013433

C.(Vervolg). VAN BELANG GEACHTE DOCUMENTEN

Categorie °	Geciteerde documenten, eventueel met aanduiding van speciaal van belang zijnde passages	Van belang voor conclusie nr.
Y	EP 1 304 030 A2 (EMBREX INC [US]) 23 april 2003 (2003-04-23)	15-17
A	* alineas [0006], [0012], [0014], [0021], [0027] - [0031], [0039]; figuren 1-4,13 *	18-26

Y	WO 00/40079 A1 (EMBREX INC [US]; HEBRANK JOHN H [US]) 13 juli 2000 (2000-07-13)	15-17
A	* bladzijde 1, regel 18 - bladzijde 4, regel 19 * * bladzijde 5, regel 26 - regel 29 * * bladzijde 6, regel 1 - regel 19 * * bladzijde 6, regel 32 - bladzijde 7, regel 4 * * bladzijde 10, regel 15 - bladzijde 11, regel 16 * * bladzijde 12, regel 27 - bladzijde 13, regel 31 * * bladzijde 14, regel 4 - regel 17 * * conclusies 24,25,32,34,37 * * figuren 3,7,8 *	18-26

1

ONVOLLEDIG ONDERZOEK
AANVULLINGSBLAD C

Octrooiaanvrage Nr.:
SN 63142
NL 2013433

Volledig onderzoekbare conclusie(s):
15-26

Niet onderzochte conclusie(s):
1-14

Reden voor de beperking van het onderzoek (niet octrooieerbare uitvinding(en)):

No search has been performed for claims 1 to 14, because claims 1 to 14 are directed to a method for treatment of the human or animal body by surgery.

Claims 1 to 14 are directed to a method for injecting a fluid into an object part, i.e. a specific location, of an egg containing an avian embryo. In the description itself the invention is said to relate to a method of using a system for delivering fluids to specific embryonic structures within a developing avian egg.

An avian egg is the zygote resulting from fertilization of the ovum. It nourishes and protects the embryo located inside and constitutes a highly complex reproductive cell comprising the necessary tissues and structures to guarantee the survival and development of the embryo. Any intervention on an egg comprising an embryo can therefore be regarded as an intervention on vital parts of a living being.

"Medical treatment" means any non-significant intentional physical or psychic intervention using means or methods of medical science performed on the human or animal body by someone who need not necessarily be a medical practitioner. It is not restricted to methods serving a direct therapeutic purpose. Accordingly, it also includes treatment for non-curative purposes such as cosmetics, termination of pregnancy, castration, sterilisation, artificial insemination, embryo transfer and transplantation, tissue removal from a living donor and treatments for experimental and research purposes.

"Surgery" further defines the nature of the treatment, rather than its purpose. Surgery is hence not limited to curative purposes. The purpose of surgery may even be non-medical for instance cosmetic, or related to agriculture. Surgery is concerned with operating on the living body, including both invasive (e.g. puncture, injection, excision, catheter insertion, endoscopy, opening of bodily cavities), and conservative (non-invasive) procedures such as repositioning or manipulating an organ or tissue without making an incision.

Claims 1 to 14 are directed to injecting vital parts of the reproductive cell containing a developing embryo. This can be regarded as an invasive procedure on the animal body, and thus a surgical treatment, since it does not result in the death of the embryo and therefore is aimed towards maintaining the life and health thereof.

The subject-matter of claims 1 to 14 is considered as an invasive, i.e. a "non-significant intentional physical intervention" on the living animal body, and thus a surgical treatment, irrespective of the underlying

purpose.

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

Informatie over leden van dezelfde octrooifamilie

Nummer van het verzoek om een onderzoek naar de stand van de techniek: NL 2013433

In het rapport genoemd octrooigeschrift	Datum van publicatie	Overeenkomend(e) geschrift(en)	Datum van publicatie
US 7165507	B2 23-01-2007	AU 2005299544 A1	04-05-2006
		BR PI0516122 A	26-08-2008
		CA 2588258 A1	04-05-2006
		CN 101048061 A	03-10-2007
		EP 1804575 A2	11-07-2007
		JP 5393625 B2	22-01-2014
		JP 2008517668 A	29-05-2008
		JP 2011005288 A	13-01-2011
		KR 20070059170 A	11-06-2007
		US 2006102082 A1	18-05-2006
		WO 2006047458 A2	04-05-2006
EP 1304030	A2 23-04-2003	GEEN	
WO 0040079	A1 13-07-2000	AT 232681 T	15-03-2003
		AU 2386600 A	24-07-2000
		BR 9916779 A	04-12-2001
		CA 2358208 A1	13-07-2000
		CN 1332603 A	23-01-2002
		DE 69905493 D1	27-03-2003
		DE 69905493 T2	18-12-2003
		DK 1139728 T3	16-06-2003
		EP 1139728 A1	10-10-2001
		ES 2196919 T3	16-12-2003
		JP 3645815 B2	11-05-2005
		JP 2002534066 A	15-10-2002
		PT 1139728 E	30-06-2003
		US 6244214 B1	12-06-2001
		WO 0040079 A1	13-07-2000

WRITTEN OPINION

File No.	Filing date *(day/month/year)*	Priority date *(day/month/year)*	Application No.
SN63142	08.09.2014		NL2013433

International Patent Classification (IPC)
INV. A01K45/00

Applicant
Viscon B.V.

This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the application
- ☒ Box No. VIII Certain observations on the application

	Examiner
	Postma, Rob

Application number

WRITTEN OPINION

NL2013433

Box No. I Basis of this opinion

1. This opinion has been established on the basis of the latest set of claims filed before the start of the search.

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ on paper

   ☐ in electronic form

   c. time of filing/furnishing:

   ☐ contained in the application as filed.

   ☐ filed together with the application in electronic form.

   ☐ furnished subsequently for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Application number

WRITTEN OPINION

NL2013433

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step, or to be industrially applicable have not been examined in respect of

☐ the entire application

☒ claims Nos. 1-14

because:

☒ the said application, or the said claims Nos. 1-14 relate to the following subject matter which does not require a search *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no search report has been established for the whole application or for said claims Nos. 1-14

☐ a meaningful opinion could not be formed as the sequence listing was either not available, or was not furnished in the international format (WIPO ST25).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; or such tables were not available in electronic form.

☒ See Supplemental Box for further details.

Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty	Yes:	Claims	19-26
	No:	Claims	15-18
Inventive step	Yes:	Claims	19-26
	No:	Claims	15-18
Industrial applicability	Yes:	Claims	15-26
	No:	Claims	

2. Citations and explanations

see separate sheet

WRITTEN OPINION

Box No. VII Certain defects in the application

see separate sheet

Box No. VIII Certain observations on the application

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

No search has been performed for claims 1 to 14, because claims 1 to 14 are directed to a method for treatment of the human or animal body by surgery.

Claims 1 to 14 are directed to a method for injecting a fluid into an object part, i.e. a specific location, of an egg containing an avian embryo. In the description itself the invention is said to relate to a method of using a system for delivering fluids to specific embryonic structures within a developing avian egg.

An avian egg is the zygote resulting from fertilization of the ovum. It nourishes and protects the embryo located inside and constitutes a highly complex reproductive cell comprising the necessary tissues and structures to guarantee the survival and development of the embryo. Any intervention on an egg comprising an embryo can therefore be regarded as an intervention on vital parts of a living being.

"Medical treatment" means any non-significant intentional physical or psychic intervention using means or methods of medical science performed on the human or animal body by someone who need not necessarily be a medical practitioner. It is not restricted to methods serving a direct therapeutic purpose. Accordingly, it also includes treatment for non-curative purposes such as cosmetics, termination of pregnancy, castration, sterilisation, artificial insemination, embryo transfer and transplantation, tissue removal from a living donor and treatments for experimental and research purposes.

"Surgery" further defines the nature of the treatment, rather than its purpose. Surgery is hence not limited to curative purposes. The purpose of surgery may even be non-medical for instance cosmetic, or related to agriculture. Surgery is concerned with operating on the living body, including both invasive (e.g. puncture, injection, excision, catheter insertion, endoscopy, opening of bodily cavities), and conservative (non-invasive) procedures such as repositioning or manipulating an organ or tissue without making an incision.

Claims 1 to 14 are directed to injecting vital parts of the reproductive cell containing a developing embryo. This can be regarded as an invasive procedure on the animal body, and thus a surgical treatment, since it does not result in the death of the embryo and therefore is aimed towards maintaining the life and health thereof.

The subject-matter of claims 1 to 14 is considered as an invasive, i.e. a "non-significant intentional physical intervention" on the living animal body, and thus a surgical treatment, irrespective of the underlying purpose.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1	US 7 165 507 B2 (WOLFE STEPHEN P [US] ET AL) 23 januari 2007 (2007-01-23)in de aanvraag genoemd
D2	EP 1 304 030 A2 (EMBREX INC [US]) 23 april 2003 (2003-04-23)
D3	WO 00/40079 A1 (EMBREX INC [US]; HEBRANK JOHN H [US]) 13 juli 2000 (2000-07-13)

The present application does not meet the criteria of patentability, because the subject-matter of independent claim 15 is not new.

D1 discloses, the reference numerals referring to this document:

A system for injecting objects, such as eggs *(10)* with a fluid, which eggs are supplied *(implicit)*, wherein said objects each comprise at least two object parts *(22, 24, 26)*, of which at least one object *(e.g. the subgerminal cavity 26)* part is to be injected. The system disclosed in document D1 is arranged to advance injection needles *(30)* to a determined depth, which depth is expected to correspond with the at least one object part to be injected *(see document D1, column 6, line 51 to column 7, line 6, where it is disclosed that the needle is inserted into the albumen of the egg and thus close to the subgerminal cavity)* into the objects and injecting fluid into the objects at the determined injection depth, monitoring pressure of the fluid by means of a sensor *(40)*

at least during injecting *(see document D1, the steps of blocks 120, 125 in Figure 4)*, and detecting an operational state of the needle and/or the fluid based on the monitored pressure *(see document D1, in particular block 125 in Figure 4, which is a step in which a pressure drop in the lumen of the needle, which lumen extends through the entire needle, is detected, thus disclosing detection of an operational state of the system)*, whereby the system has a controller.

Independent claim 15 therefore lacks novelty as all features thereof are known from document D1.

The present application does not meet the criteria of patentability, because the subject-matter of independent claim 15 does not involve an inventive step.

D2 may be regarded as being the prior art closest to the subject-matter of claim 15, and discloses, the reference numerals referring to this document:

A system for injecting objects, such as eggs *(20)* with a fluid, which eggs are supplied *(eggs are supplied via flat 15)*, wherein said objects each comprise at least two object parts *(implicit)*, of which at least one object part is to be injected. The system disclosed in document D2 is arranged to advance injection needles *(90)* to a determined depth, which depth is expected to correspond with the at least one object part to be injected *(see document D2, column 8, lines 35 to 38 or column 10, lines 25 to 34)* into the objects and injecting fluid into the objects at the determined injection depth, whereby the system has a controller *(100)*.

The subject-matter of claim 15 therefore differs from this known system in that the pressure of the fluid is monitored by means of a sensor at least during injecting, and in that an operational state of the needle and/or the fluid based on the monitored pressure is detected.

The effect of these distinguishing features is that the needle can be positioned more accurately within the object part to be injected with fluid, and/or that the correct position of the needle within the object part to be injected with fluid can be confirmed.

The objective technical problem to be solved by the present invention may therefore be regarded as how to modify the system known from D2 such that accuracy is improved and the correct positioning of the needle can be confirmed.

The solution proposed in claim 15 of the present application cannot be considered as involving an inventive step for the following reasons:

When looking for a solution to the objective technical problem the person skilled in the art would come across document D3, as this document relates to a method and system for injecting a plurality of eggs and deals with the problem of controlling depth penetration of the injection needle into the eggs.

More in particular document D3 *(see e.g. document D3, page 10, line 15 to page 11, line 16)* teaches the skilled person to provide a pressure detector (110) to monitor the pressure of the fluid and to detect an operational state of the fluid on the basis of the pressure detected so as to sense the depth of the needle inside the egg.

Hence, when looking for a solution for the objective technical problem the person skilled in the art would learn from document D3 how to modify the system known from document D2 without the need for further modifications and without needing any inventive skill.

Independent claim 15 therefore lacks inventive step in view of what is known from document D2 in combination with what is known from document D3.

Dependent claims 15-18 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of novelty and/or inventive step as the subject-matter of these claims is disclosed in document D1 (claims 15-18) or rendered obvious in light of a combination of documents D2 and D3 (claims 15-17).

The subject-matter of dependent claims 19-26 is neither known nor suggested by the prior art mentioned in the search report.

Re Item VII

Certain defects in the application

The relevant background art disclosed in documents D1, D2 and D3 is not mentioned in the description, nor are these documents identified therein.

The features of the claims are not provided with reference signs placed in parentheses.

Re Item VIII

Certain observations on the application

The statement in the description on page 10, lines 27-32 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity when used to interpret them.

The following typographical errors were observed in the application:

On page 1, line 23, "injecting a objects" has been understood as "injecting objects".

On page 6, line 32, "for example of vessel" has been understood as "for example a vessel".