Abstract: In one embodiment, the present invention provides an intrauterine device (IUD) comprising an oval shape, wherein the device comprises a core of magnetic material, an inert material or copper coating the core, wherein the coating comprises a pharmaceutical agent, copper or a combination thereof. Another embodiment provides a method to suppress estrus in a subject comprising inserting an intrauterine device (IUD) comprising an oval shape, wherein the device comprises a core of magnetic material and an inert material or copper coating the core.
INTRAUTERINE DEVICE (IUD)

Cross-Reference to Related Application

This application claims priority to U.S. Provisional Application Serial No. 62/091,387, filed on December 12, 2014, which is incorporated by reference herein in its entirety.

Background of the Invention

Mares come into heat or estrus due to rising estrogen levels, which are produced by developing ovarian follicles. Mares typically do not show heat during the winter or after ovulation. The expression of behavioral estrus occurs in the presence of estrogen and the absence of progesterone; while the absence of estrus is a function of low estrogen levels and/or elevated progesterone levels.

During the estrous cycle, mares can behave in a manner that can make riding, training, competing, or handling these horses difficult. Currently, most methods to attempt to suppress estrus behavior during the breeding season, when most horse competing events take place, include pharmacological and negative reinforcement strategies.

With regard to pharmacological therapies, a common strategy is to give a horse synthetic progesterone compounds, which are administered every day. However, there are risks involved with this approach. The most common product used is altrenogest (Regu-mate®). This product must be given daily and orally to horses. If it comes in contact with the handler, it is rapidly absorbed through the skin and becomes an endocrine disruptor in women, and/or contaminates the environment. Another pharmacological therapy includes injections of medroxyprogesterone acetate (Depo-Provera®). Study results have shown that administering this drug to mares with the goal of suppressing estrus is not effective.

Regarding physical therapies, negative reinforcement is an approach in use by some riders to try to mitigate estrus behavior, as well as pregnancy/termination approaches.
Another strategy is the use of 35-45 mm glass marbles placed in the uterus of mares (thought to extend the function of the corpus luteum). It is believed that when a marble is placed in the mare’s uterus, pregnancy recognition ensues and estrus is suppressed. This procedure has limited success because the majority of the marbles are expelled from the uterus prematurely (estrus is suppressed in only about 40% of mares for 60 to 90 days). Another drawback of this procedure is that in some mares, once the marble is placed in the uterus, they are very difficult to retrieve, therefore limiting its use in potential brood mares (limiting the ability to reverse the procedure).

**Summary of the Invention**

During the natural breeding season in the northern hemisphere, February through September, estrus/heat and subsequent ovulation and estrus behavior occur for a week length of estrogen dominance, followed by 2 weeks of progesterone dominance, wherein the mares do not show any unwanted signs of heat/estrus behavior. In general, the estrous cycle is monitored by teasing to a stallion, by measurement of estrogen/progesterone in the blood and/or by ultrasound.

One embodiment of the invention provides for the control of the estrous cycle without the use of drugs (e.g., that may affect the handler, contaminate the environment and/or potential harm to the animal). One embodiment provides an easily retrievable inert contraceptive device with high retention rate, such as weeks, months and even years or for the duration of the breeding season without affecting future fertility.

The oval shaped (optionally medicated) estrus suppressing IUD is generally for veterinary, such as in mares, and non-veterinary use. The IUD is magnetic. Further provided is a magnetic wand to facilitate removal of the IUD (and optionally insertion).

One embodiment provides an intrauterine device (IUD) comprising an oval shape, wherein the device comprises a core of magnetic material, an inert material coating the core, wherein the coating comprises an optional pharmaceutical agent. In one embodiment, the core comprises iron, nickel,
cobalt, an alloy of rare earth metal, or a naturally occurring mineral. In one embodiment, the core comprises neodymium. In one embodiment, the coating comprises Teflon®, silicon, polymers, elastomers, copper or a combination thereof. In another embodiment, the coating comprises polyethylene or polypropylene. In one embodiment, the pharmaceutical agent is progesterone, progestogen, copper or a combination thereof (cytotoxic anti-fertility effect). In another embodiment, the pharmaceutical agent is slow releasing. In one embodiment, the IUD is about 20mm to about 50mm in length and about 1mm to about 20mm in width. For example, in one embodiment, the length of the device is about 10mm to about 30mm and the width is about 1mm to about 15mm. In one embodiment, the device comprises more than one IUD. In another embodiment, the device comprises 2 or 3 IUDs (each about 10mm to about 100mm in length to about 1mm to about 20 or 30mm in width).

One embodiment provides a method to suppress estrus (and/or prevent pregnancy) in a subject comprising inserting the device described herein. In one embodiment, the retention rate for the desired period of time for suppressing estrus is at least about 90%, at least about 95%, or at least about 99%. In one embodiment, the retention rate is 100%. In one embodiment, the device comprises more than one IUD, such as 2 or 3, wherein the IUDs self-aggregate after insertion in the uterus (remote self assembly).

One embodiment provides a method to remove an IUD as described herein from the uterus of a subject comprising retrieving said IUD with a magnetic retrieving wand, wherein the diameter of the wand is such that it can pass into the uterus of said subject.

Another embodiment provides a kit comprising the IUD as described herein and a magnetic retrieving wand, wherein the diameter of the wand is such that it can pass into the uterus of a subject. The kit can comprise more than one IUD.

**Brief Description of the Drawings**

Figure 1 depicts the IUD (10) and a picture of a marble (20).
Figure 2A-C depicts the retriever wands (30) and cups/magnetic ends (32) of the wand (31).

Figure 3 depicts an ultrasound image of the uterus of a mare. The left panel depicts the shadow caused by the device (IUD; 10).

Figure 4 depicts several possible configurations of 2-3 IUDs (10) that may self-aggregate in the uterus.

Figure 5 depicts an example of an inserter/applicator (40).

Figure 6 depicts magnetic ends (32) of the wand (31).

**Detailed Description**

**Definitions:**

In describing and claiming the invention, the following terminology will be used in accordance with the definitions set forth below.

The articles "a" and "an" are used herein to refer to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

The term "about," as used herein, means approximately, in the region of, roughly, or around. When the term "about" is used in conjunction with a numerical range, it modifies that range by extending the boundaries above and below the numerical values set forth. In general, the term "about" is used herein to modify a numerical value above and below the stated value by a variance of 10%. In one aspect, the term "about" means plus or minus 20% of the numerical value of the number with which it is being used. Therefore, about 50% means in the range of 45%-55%. Numerical ranges recited herein by endpoints include all numbers and fractions subsumed within that range (e.g. 1 to 5 includes 1, 1.5, 2, 2.75, 3, 3.90, 4, and 5). It is also to be understood that all numbers and fractions thereof are presumed to be modified by the term "about."

"Pharmaceutically acceptable" means physiologically tolerable, for either human or veterinary application.

As used herein, "pharmaceutical compositions" include formulations for human and veterinary use.
"Plurality" means at least two.

As used herein, a subject can be a female animal, including a mammal, such as a human, or a domestic animal, including a horse, dog, cow, goat, or cat, or wild carnivores, such as wolf, bear, cheetah, tiger, leopard, lion; or ruminants/pseudo ruminants such as camels, deer, antelope, buffaloes; or large mammals such as elephants.

Embodiments

IUD

In some embodiments, the IUD (10) is oval (having a rounded and slightly elongated outline or shape, like that of an egg; elliptical; ellipsoidal configuration). The device (10) can range in size from about 1mm to about 100mm; for example, the device (10) can range from about 10mm to 100mm in length and about 1mm to 30mm in width. In one embodiment, the device (10) has a weight of about 1g to about 100g. For example, for a horse or cow, the size of the IUD (10) can be about 20mm to about 50mm in length and about 10mm to about 20mm in width. For a cat or small dog, the size of the IUD (10) can be about 5mm to about 10mm in length and about 2mm to about 5mm in width. For larger animals, such as a large dog, goat or sheep, the size of the IUD (10) can be about 6mm to about 25mm in length and about 3mm to about 15mm in width. In primates (e.g., human), the length of the device (10) is about 10mm to about 30mm and the width is about 3mm to about 15mm.

The core of the device (10) can comprise magnetic material (a piece of iron (or an ore, alloy, or other material) that has its component atoms so ordered that the material exhibits properties of magnetism, such as attracting other iron-containing objects or aligning itself in an external magnetic field). For example, the core of the device (10) can comprise materials that are magnetized (called ferromagnetic or ferrimagnetic). These include iron, nickel, cobalt, some alloys of rare earth metals (including neodymium), and some naturally occurring minerals such as lodestone.

In some embodiments only one IUD (10) is inserted in the subject. In other embodiments, more than one is inserted. When more than one IUD (10) is
inserted, the each IUD (10) may be smaller (than if only using one), as the IUDs (10) will self-assemble into a larger IUD (10) internally (in uterus) due to the magnetic qualities of the IUD (10; they self-assemble in the uterus like pearls of a necklace or a compass rose). In one embodiment, 1-3 IUDs (10) are used. The size and number can be dependent on the species (human, domestic animal, wildlife). For example, when multiple IUDs (10) are inserted the size of each IUD (10) is individually about 3mm to about 30mm in length and about 2mm to about 15mm in width. This smaller size enables the placement of the IUD (10) in the uterus at any stage of the cycle and still retain high retention rates, such as about 90%, about 95%, about 99%, 100% retention rates.

The core is covered with a nontoxic and physiologically acceptable material such as Teflon®, silicon, polymers, polyethylene, polypropylene or elastomers. In general, any coating available to an art worker suitable for in uterus use is acceptable for the inventions herein. There are many coatings known in the art.

In one embodiment, the IUD (10) contains an anti-fertility agent, such progesterone, and is permeable to passage of the anti-fertility agent at a low rate. Upon insertion in the uterus, the device (10) releases a fertility suppressing amount of the anti-fertility agent to the uterus. In one embodiment, the coating can optionally include (mixed or coated thereon) a pharmaceutically acceptable agent including, but not limited to, progesterone, progestogen, levonorgestrel or a combination thereof, such as slow release progesterone, progestogen and/or levonorgestrel. The device (10) may also include copper (such as copper rings or ridges (40) on the outside of the IUD (10), protruding above the surface or embedded in the coating so as to be flush with the surface or a portion or entire outer coating of the IUD (10) can be copper).

The color of the device (10) is optional.

One embodiment provides for grooves (40, indentation) of about 1mm to about 3mm in size on the outside of the IUD (10) or ridges (40; protrusions; ribs/rings (which can comprise copper)) of about 1mm to about 3mm in size on the outside of the device. In one embodiment, the grooves (40) or ridges (40) are longitudinal (spanning the length of the body), laterally (spanning the width
of the body) or a combination thereof. The protrusion or indentations can facilitate retention of the device (10).

One embodiment of an IUD (10) of the invention is the 50x20 mm egg-shaped Teflon coated magnetic bar available from Scienceware, Wayne, NJ 07470 (Figure 1).

One embodiment provides that an ultrasound of the uterus is performed two dimensional/three dimensional to determine its health, non-pregnancy, and dimensions to aid in the choice of size of the IUD (10) to be used. If self-inserted, the minimum precaution is to establish non-pregnancy. If tail string is used in the IUDs (10) for self-retrieval, the materials can be polypropylene or polyethylene.

Another embodiment provides for an ellipse shape and a smooth surface. In one embodiment, if more than IUD is present, the IUDs may be threaded to each other with a monofilament (e.g., similar to fishing line) with one IUD having a longer tail for retrieval of the IUDs. Size ranges are according to those discussed herein.

Examples:

Item: R750B-PTFE
Material: NdFeB Magnet with PTFE coating
Grade: N40
Magnetization: Length
Dimensions: 26mm Length x 12mm Max Diameter
Shape: Ellipse
Tolerance: +/-.2mm

Item: R750C-PTFE
Material: NdFeB Magnet with PTFE coating
Grade: N40
Magnetization: Length
Dimensions: 32.5mm Length x 15mm Max Diameter

Shape: Ellipse

Tolerance: +/- .2mm

Inserter/Applicator

Self or assisted insertion can hand can be carried out.

Further, a device (40) can be used for insertion. For example, a device (40) with the variable dimensions, such as variable length/diameter. For example, for horses a 75 cm plunger with a polystyrene casing/applicator 75 mm in length and 14 mm width (Figure 5; (40)). In one embodiment, the applicator (40) can accommodate IUD(s) (10) in line, inserted in cervix - ejected by a plunger.

Retrieving Wand

One embodiment provides a retrieving wand (30). The wand (30) is of a diameter that can pass through the cervix of the female subject. For example, the wand (30) can be 5cm to about 350cm in length and about 1mm to about 20mm in diameter. Generally, the wand (30) comprises a magnet (32; as discussed above for the IUD (10)) at one end encapsulated by an inert coating such as polypropylene or Polytetrafluoroethylene (PTFE). The attractive force between the magnet of the IUD (10) and the magnetic wand (30) inserted into the uterus will be sufficient to allow removal of the magnetic IUD (10) from the uterus with the magnetic wand i.e., by magnetic attractive forces.

One embodiment of the retrieving wand (30 of the invention is the magnetic retriever wand available from Scienceware, Wayne, NJ 07470 (Figure 2A-C).

In one embodiment, the retriever (30) is stainless steel of variable length. In one example, the retriever (30) has a 3 mm thickness, 85 cm long (descriptions of the sizes of the retriever/wand (30) provided herein apply here as well). In one embodiment, the end of the retriever (30) will have a thread to accommodate variable dimensions of the female threaded size cups/magnets (32). Variable pulling capacity up to 10 Kg. The cups/magnets (32) will be neodymium magnets embedded in a durable stainless steel housing. Steel
housing absorbs the South polarity and wraps it to face the other direction increasing the attach/pull strength. Thus stronger because the South Pole is redirected to face north. Some example dimensions (see Figure 6; (32): A | Diameter: 15.88mm; B | Height: 13.00mm; C | Post Height: 8.00mm; D | Thread Depth: 3.94mm; E | Post Diameter: 8.00mm; Surface Gauss: 401 1; Max Pull: 9.19 kg.

Retrieval can also be carried out by a tail, e.g., a length of filament or string hanging/connected to an IUD (10) (similar to removal of other IUDs).

**Detection**

Detection of the IUDs (10) can be done by ultrasound or Gauss meter/metal detector.

The following examples are intended to further illustrate certain particularly preferred embodiments of the invention and are not intended to limit the scope of the invention in any way.

**EXAMPLES**

During the breeding season, in the spring and summer, mares ovulate every 18-24 days - average 21 days. A typical mare has 5-7 days of estrus/receptivity - estrogen dominance- followed by 14 days of diestrus/non receptivity - progesterone dominance. Ovulation occurs 2 days before the end of estrus. Day of ovulation is Day 0.

Mares will be routinely teased and evaluated by ultrasound (US) to determine their reproductive status and stage of the cycle. With the use of transrectal US one is able to follow the ovarian follicular dynamics and determine the day of ovulation. Within 48 hrs post ovulation the cervix will close/tighten, but still allow for the introduction of an IUD (10), with the highest rate of retention. Breaching the cervix after 48 hrs post ovulation, during progesterone dominance, can lead to uterine infection with the subsequent expulsion of the IUD (10). Up to 48 hours post-ovulation, during transition from estrogen to progesterone dominance, the uterus is not as susceptible to infection and contamination.
Example I

Six mares were used as clinical patients during the breeding season. An IUD (10), as described herein, was placed in the uterus 24-48 hours after ovulation. At the time of the IUD (10) insertion, 2.4g of the anti-bacterial Timentin® (GlaxoSmithKline, UK) diluted in 10ml of sterile saline, was infused into the uterus. The retention rate for three months was 100%. The devices (10) were visualized monthly by ultrasound in the uterus (Figure 3; left panel). No signs of estrus were observed for the duration of the uterine implant. After three months, the devices (10) were recovered with ease with three mares and the mares returned to their regular cycles and behavior. Ultrasound scans of the uteri were normal. The oval shape of the device (10) does not appear to distort the uterine lumen, thus reducing the likelihood of side effects. Three other mares had longer in uterus exposure with 100% retention rates.

Example II

About 15 horses, each of them being their own control, will be further studied. Maiden versus non-maiden mares, as to IUD (10) retention, will be investigation as well.

Biopsy

The procedure will take about 30 minutes for a uterine pinch biopsy (1 linear cm of tissue; a routine clinical procedure in horses; with sedation/analgesia) and insertion/retrieval of IUD (10). A biopsy (sterilized) instrument (Pilliag Surgical Instrument Co, Fort Washington, PA 19034) will be used to collect endometrial specimens. Before the procedure, 2-4 mg of detomidine hydrochloride can be administered intravenously as a sedative and analgesic. The mare's perineum will be scrubbed with a mild antiseptic bethadine solution before digital insertion of the biopsy instrument through the vagina and cervix. The specimens (two samples per mare - one at the beginning of the study and the other at the end) obtained will be 10x3x3 mm in size and will be pinched from the base of one of the uterine horns (RM Kenney and PA Doig. Current Therapy in Theriogenology. Ed David Morrow, p 723-729, 1986, WB Sounders). Specimens will be placed immediately in 10% buffered formalin for histologic evaluation.
IUD insertion

The implant and equipment used for insertion would be sterilized before beginning the procedure. The mare's perineum will be scrubbed with a mild antiseptic betadine solution before digital insertion of the sterilized IUD (10) (50x20 mm egg-shaped teflon coated magnetic bar; Scienceware, Wayne, NJ 07470; Figure 1) through the vagina and cervix. Because the mare will be within 2 day post ovulation, thus technically in estrus/receptive, her cervix will be pliable and allowing the introduction of the IUD (10) with minimum effort. It is noted that in horses the stallion does ejaculate directly into the uterus, thus the cervix of a mare in estrus is able to accommodate a glans penis of a stallion.

Ultrasound/Blood Sampling

Mares will be ultrasounded every month post IUD (10) placement.

Ten ml of blood will be collected from the jugular vein of each horse into a red top vacutainer tube. Samples will be collected on the day of the IUD (10) insertion, and then once a month until the day the mare is induced to return to estrus for IUD (10) retrieval. The rational to sample for progesterone is to show that the presence of the IUD (10) induces a state of pseudo-pregnancy by preventing the mare to return to normal cycle, as long as the IUD (10) is in place and progesterone is above base line i.e., 0.5-Ing/ ml.

IUD retrieval

On day 90 (short term group) or in the next breeding season (long term group) post IUD (10) insertion mares will be induced to return to estrus by injecting 250 micrograms of prostaglandin (cloprostenol-Schering-Plough, TN 02012) IM. After the injection the mares are expected to return to estrus within 2-3 days and the cervix will be relaxed. At this time the IUD (10) will be retrieved through the cervix with a magnetic retriever wand (Scienceware, Wayne, NJ 07470; Figure 2). The mare's perineum will be scrubbed with a mild antiseptic betadine solution before digital insertion of the magnetized wand (30) through the vagina and cervix. (In the unlikely event that the IUD (10) would not be retrieved with the magnetized wand, it would be removed manually after
dilation of the cervix with or without the use of 3 mg of misoprostol PGE1 (Pfizer)).

No clinical effects are expected after the retrieval of the IUD (10). However, dangerous mare behavior patterns that put horse riders and handlers at risk may recur associated with regular return to cyclicity.

Timeline

Each mare will be biopsied 2 days after the beginning of estrus. The IUD (10) will be inserted two days after ovulation (Day 2). The mares in two groups: maiden/non-maiden blood sampling will be done on Day 2, and monthly thereafter; with the last sampling on the day the mare is given prostaglandin to relax the cervix for IUD (10) retrieval.

Group A - 8 mares - Short term IUD

A blood sample will be collected from the jugular vein and submitted for progesterone analysis at the time of IUD (10) insertion, and every 30 days for up to three months. On day 90 post IUD (10) insertion, the last blood sample will be collected and the mares will be induced to return to estrus. After the injection the mares are expected to return to estrus within 2-3 days. At this time the IUD (10) will be retrieved through the cervix with a magnetic retriever wand (30). To demonstrate any effect of the IUD (10) on the lining of the uterus, a paired biopsy sample will be collected before and immediately after IUD (10) retrieval. Three mares will be inserted with 3 IUDs (10) of 30mm in length and 16mm in width, as a model for primates (e.g., human) use.

Group B - 7 mares - Long term IUD

The only difference between this group and the previous group protocol is that the IUD (10) in this group will be kept in place until the following breeding season, up to 1 year total. Monthly assay of progesterone and ultrasound exams/metal detector (e.g., hand held metal detector purchased from, for example, CEIA USA Ltd., Twinsburg, OH) will be conducted as described above.
Headings are included herein for reference and to aid in locating certain sections. These headings are not intended to limit the scope of the concepts described therein under, and these concepts may have applicability in other sections throughout the entire specification.

The invention is described with reference to various specific and preferred embodiments and techniques. However, it should be understood that many variations and modifications may be made while remaining within its scope. All referenced publications, patents and patent documents are intended to be incorporated by reference, as though individually incorporated by reference.
WHAT IS CLAIMED IS:

1. An intrauterine device (IUD) comprising an oval shape, wherein the device comprises a core of magnetic material, an inert material or copper coating the core, wherein the coating comprises a pharmaceutical agent, copper or a combination thereof.

2. The device of claim 1, wherein the core comprises iron, nickel, cobalt, an alloy of rare earth metal, or a naturally occurring mineral.

3. The device of claim 2, wherein the rare earth metal is including neodymium.

4. The device of claim 1, wherein the coating comprises Teflon®, silicon, polymers, or elastomers.

5. The device of claim 4, wherein the polymer is polyethylene or polypropylene.

6. The device of claim 1, wherein the pharmaceutical agent is progesterone, progestogen, copper or a combination thereof.

7. The device of claim 1, wherein the pharmaceutical agent is slow releasing.

8. The device of 1, wherein the IUD is about 1mm to about 30mm in width and about 10mm to about 100mm in length.
9. The device of claim 1, wherein the device comprises more than one IUD.

10. The device of claim 9, wherein the device comprises 2 or 3 IUDs.

11. A method to suppress estrus in a subject comprising inserting the device of claim 1.

12. A method to suppress estrus in a subject comprising inserting an intrauterine device (IUD) comprising an oval shape, wherein the device comprises a core of magnetic material and an inert material or copper coating the core.

13. The method of claim 12, wherein the coating comprises a pharmaceutical agent.

14. The method of claim 11, wherein the retention rate for the desired period of time is at least about 90%, at least about 95%, or at least about 99%.

15. The method of claim 14, wherein the retention rate is 100%.

16. The method of claim 11, wherein the device comprises more than one IUD, wherein the IUDs self-aggregate after insertion in the uterus.
17. A method to remove an IUD of claim 1 from the uterus of a subject comprising retrieving said IUD with a magnetic retrieving wand, wherein the diameter of the wand is such that it can pass into the uterus of said subject.

18. A method to remove an IUD from the uterus of a subject comprising retrieving said IUD with a magnetic retrieving wand, wherein the diameter of the wand is such that it can pass into the uterus of said subject, wherein the IUD comprises an oval shape, wherein the device comprises a core of magnetic material and an inert material or copper coating the core.

19. A kit comprising the IUD of claim 1.

20. The kit of claim 19, further comprising a magnetic retrieving wand, wherein the diameter of the wand is such that it can pass into the uterus of a subject.
FIG. 2B
FIG. 6
# INTERNATIONAL SEARCH REPORT

## A. CLASSIFICATION OF SUBJECT MATTER

**IPC(8)** - A61 F 6/14 (2015.01)

**CPC** - A61F 6/14

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 (8):** A61F 6/14 (2015.01)

**CPC:** A61F 6/14

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

**IPC (8):** A61F 6/14, A61F 6/18, A61F 6/06, A61 F 6/00 (2015.01); **CPC:** A61F 6/14, A61F 6/18, A61F 6/06; **UC:** 128/833, 128/830

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

PatBase, Google Patent, Google Scholar

Search terms used: IUD magnetic core intrauterine device oval shaped marble ball equine iron nickel multiple devices aggregate magnet "cobalt alloy egg elliptical ellipsoidal coat" each metal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>US 3,993,057 A (Ramwell) 23 November 1976 (23.1.1976), Entire document</td>
<td>1-2, 4-15</td>
</tr>
<tr>
<td>Y</td>
<td></td>
<td>3, 17-20</td>
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<tr>
<td>A</td>
<td></td>
<td>16</td>
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<tr>
<td>Y</td>
<td>CN 1228297 A (Shulan et al.) 15 September 1999 (15.09.1999), Entire document</td>
<td>3</td>
</tr>
<tr>
<td>Y</td>
<td>US 3,908,646 A (Ansari) 30 September 1975 (30.09.1975), fig 3, col 4</td>
<td>17-20</td>
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</tbody>
</table>

Further documents are listed in the continuation of Box C.

* 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 application or patent 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

Date of the actual completion of the international search:
07 January 2016 (07.01.2016)

Date of mailing of the international search report:
29 JAN 2016

Name and mailing address of the ISA/US:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
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Facsimile No. 571-273-8300

Authorized officer:
Lee W. Young

PCT/ISA/210 (second sheet) (January 2015)