

【DESCRIPTION】**【Invention Title】**

WORKSTATION FOR CRYO TRANSMISSION ELECTRON MICROSCOPE

【Technical Field】

5 The present invention relates, in general, to a workstation for cryogenic transmission electron microscopy, in which a biological sample is observed at low temperature using a transmission electron microscope or a high-voltage electron microscope (HVEM) and, more particularly, to a workstation for cryogenic transmission
10 electron microscopy, in which a biological sample processed at low temperature is more rapidly and efficiently loaded onto a holder of the workstation, thereby making it possible to improve efficiency and reliability of the
15 cryogenic transmission electron microscopy during which it is important to maintain the low temperature.

【Background Art】

Recent science and engineering technologies take an interest in the submicrometer microstructure of a material
20 departing from a process. Thus, an instrument, such as a transmission electron microscope or an atomic force microscope (AFM), which can directly observe the microstructure, and technologies using such an instrument are being greatly developed. Technologies that directly
25 observe organic materials such as polymers or biological

samples using the transmission electron microscope also arouse much interest. Particularly, the direct observation of the organic materials using the transmission electron microscope, etc. is more difficult compared with the
5 observation of inorganic materials. This is because the organic materials have a melting point lower than the inorganic materials. Thus, when a sample of the organic material is prepared, physical chemical processing such as staining is required.

10 Among the organic materials, the present invention is mainly interested in technology that processes a biological sample such as a cell into a sample capable of direct observation using the transmission electron microscope or a high-voltage electron microscope (HVEM). There are several
15 methods of processing the biological sample, for example, a staining method of drying the biological sample and staining the dried biological sample, a chemical fixation method of injecting and fixing a fixing solution into a fine cell structure, and so on. However, in the case of
20 the staining method, the staining itself is impossible for certain kinds of biological samples, or a staining agent deforms a structure of the biological sample making it difficult to observe a prototype of the biological sample. In the case of the chemical fixation method, the speed at
25 which a fixing solution is penetrated into a cell is slow,

and thus it is difficult to observe a cell structure the way the prototype should be, and its processing is complicated.

A technique developed in order to overcome these
5 drawbacks of the related arts is to rapidly cool a biological sample using liquid nitrogen or liquid helium to maintain a prototype of the biological sample without deformation, and then observe the biological sample using, for instance, a transmission electron microscope. This
10 technique is commonly called "cryogenic transmission electron microscopy (cryo-TEM)," and its availability is known through several monographs.

In order to use the cryo-TEM, the biological sample must be rapidly frozen without deformation using a
15 vitrification device, for instance a VitrobotTM device available from FEI Company, and then be loaded onto the holder of a workstation under low temperature. The sample loaded onto the holder through this process is inserted into a transmission electron microscope for observation.

20 FIG. 1 illustrates a conventional workstation 1 used when a rapidly frozen sample is loaded onto a holder under low temperature. The workstation 1 generally includes a stand 11, an insulated vessel 12 disposed on one side of an upper surface of the stand 11, and a Dewar vessel 13
25 disposed on the other side of the stand 11. A transparent

cover 17, having a sample loading port 18 and a liquid nitrogen injection port 19, is detachably mounted on an upper end of the insulated vessel 12. A holder insertion socket 16 is formed on a sidewall of the insulated vessel 12 which faces the Dewar vessel 13. Similarly, the Dewar vessel 13 is provided with a holder coupling hole 20 at a position opposite the holder insertion socket 16. The Dewar vessel 13 includes a charging port (not shown) capable of charging liquid nitrogen and a cap 14 capable of opening and closing the charging port at an upper end thereof. A holder 15 mounted on a transmission electron microscope is fitted into the holder insertion socket 16 and the holder coupling hole 20, and is kept cold by liquid nitrogen charged into the insulated vessel 12 and the Dewar vessel 13. After the workstation 1 is set, the biological sample rapidly cooled by the vitrification device is loaded onto an end of the holder 15 through the sample loading port 18 using tweezers.

However, the conventional workstation having the aforementioned configuration has the following problems.

First, when the biological sample is loaded onto the holder, water vapor in the atmosphere is cooled due to the low temperature of the liquid nitrogen, so that a freezing phenomenon occurs on the top of the transparent cover. In the case in which this freezing phenomenon occurs, a clear

field of vision is not ensured when the sample is loaded onto the end of the holder through the sample loading port, and thus loading work is delayed. This delay inevitably incurs damage to the sample. However, in order to eliminate
5 the freezing phenomenon, a method of heating the transparent cover or a method of loading the sample in a moisture-free environment, for instance under vacuum has never been adopted. As such, a new means capable of avoiding the freezing phenomenon must be found.

10 Second, in order to maintain airtightness between the holder and the holder insertion socket, an O-ring made of rubber material is interposed between the holder and the holder insertion socket. When this rubber O-ring comes into contact with the low-temperature liquid nitrogen, the
15 O-ring becomes rigid making it difficult to maintain the airtightness, and it takes a long time to separate the holder from the holder insertion socket. Further, the moisture and liquid nitrogen in the insulated vessel mix to generate blocks of ice during the process of charging the
20 liquid nitrogen into the insulated vessel. When these ice blocks become attached to the sample, it is difficult to obtain and observe a desired image from the sample through the transmission electron microscope. Thus, a means capable of properly adjusting the behavior of the liquid
25 nitrogen charged into the insulated vessel is also

required.

【Disclosure】

【Technical Problem】

Accordingly, the present invention has been made in an
5 effort to solve the problems occurring in the related art,
and an embodiment of the present invention is to provide a
workstation for cryogenic transmission electron microscopy,
which is configured to eliminate a freezing phenomenon
occurring on the top of a transparent cover when water
10 vapor in the atmosphere is cooled due to a low temperature
of liquid nitrogen when a rapidly frozen sample is loaded
onto a holder under low temperature.

Another embodiment of the present invention is to
provide a workstation for cryogenic transmission electron
15 microscopy, which is configured to not only efficiently
protect an O-ring made of rubber material interposed
between a holder and a holder insertion socket from low-
temperature liquid nitrogen but also to prevent a sample
from being contaminated by blocks of ice generated on the
20 top of a transparent cover generated by the mixing of
moisture with liquid nitrogen in an insulated vessel in the
process of charging the liquid nitrogen into the insulated
vessel.

【Technical Solution】

25 In order to achieve the above object, according to a

first embodiment of the present invention, there is provided a workstation for cryogenic transmission electron microscopy, which includes: a stand, upper and lower surfaces of which are flat; an insulated vessel disposed on one side of the upper surface of the stand, and including a holder insertion socket on a sidewall thereof, wherein a transparent cover having a liquid nitrogen injection port and a sample loading port is detachably mounted on an upper end of the insulated vessel, and includes a step on an outer circumference of an upper surface thereof; a Dewar vessel disposed on another side of the upper surface of the stand so as to face the holder insertion socket, including a charging port for charging liquid nitrogen and a cap for opening and closing the charging port at an upper end thereof, and having a holder coupling hole in a sidewall thereof which faces the insulated vessel; and a holder, opposite ends of which are coupled to the holder insertion socket and the holder coupling hole.

With this configuration, a step is formed along the outer circumference of the upper portion of the transparent cover, so that the space, in which the liquid nitrogen discharged from the interior of the insulated vessel can be confined, is formed. The liquid nitrogen, which is confined in a space of the upper portion of the transparent cover, serves as the boundary layer for preventing moisture

in the atmosphere from being frozen on the upper surface of the transparent cover. Thus, when the biological sample is loaded onto the holder, the sample can be rapidly loaded without damage in a state in which a clear field of vision
5 is ensured. Consequently, the first object of the present invention is accomplished by this configuration.

According to another embodiment of the present invention, the transparent cover is made of acryl. Besides the acryl material, any plastic material will do as long as
10 it can be used at low temperature.

According to another embodiment of the present invention, the workstation further includes a height adjuster, which is disposed on the lower surface of the stand on which the Dewar vessel is disposed. The height
15 adjuster functions to incline the stand such that the height at which the Dewar vessel is installed is higher than that at which the insulated vessel is installed. In this way, when the height adjuster inclines the stand such that the installation height of the Dewar vessel is higher
20 than that of the insulated vessel, the liquid nitrogen can be prevented from coming into direct contact with the O-ring interposed between the holder and the holder insertion socket, and the blocks of ice generated by mixing of the moisture with the liquid nitrogen in the insulated vessel
25 can be collected on the side opposite the sample because of

the inclination of the stand, and thus the sample can be prevented from being contaminated. Consequently, the second object of the present invention is accomplished by this configuration.

5 According to another embodiment of the present invention, the height adjuster includes two short rods, each of which has a regular hexagonal cross section, and a long rod connecting the two short rods at a position deviating from the center of the regular hexagonal cross
10 section of each short rod in a direction perpendicular to one of six sides of the regular hexagonal cross section of each short rod, and having a circular cross section. The long rod is in contact with the lower surface of the stand. Since the long rod deviates from the center of the regular
15 hexagonal cross section of each short rod, height of the long rod can be adjusted in four steps.

【Advantageous Effects】

According to embodiments of the present invention, the step is formed along the outer circumference of the upper
20 portion of the transparent cover having the sample loading port, so that there is formed a space inside which the liquid nitrogen discharged from the interior of the insulated vessel can be confined. The liquid nitrogen, which is confined in a space of the upper portion of the
25 transparent cover, serves as the boundary layer for

preventing moisture in the atmosphere from being frozen on the upper surface of the transparent cover. Thus, when the biological sample is loaded onto the holder, the sample can be rapidly loaded without damage in a state in which a
5 clear field of vision is ensured.

Further, the height adjuster is disposed on the lower surface of the stand on which the Dewar vessel is disposed, and functions to incline the stand such that the height at which the Dewar vessel is installed is higher than that at
10 which the insulated vessel is installed. Thereby, the liquid nitrogen can be prevented from being directly contacted with the O-ring interposed between the holder and the holder insertion socket, and the blocks of ice generated by the mixing of the moisture with the liquid
15 nitrogen in the insulated vessel can be collected on the side opposite the sample because of the inclination of the stand, and thus the sample can be prevented from being contaminated.

【Description of Drawings】

20 FIG. 1 is a cross-sectional view illustrating a conventional workstation for cryogenic transmission electron microscopy;

FIG. 2 is a cross-sectional view illustrating a workstation for cryogenic transmission electron microscopy
25 according to an exemplary embodiment of the present

invention; and

FIG. 3 is a detailed view illustrating a height adjuster according to an exemplary embodiment of the present invention.

5 **【Best Mode】**

Hereinafter, a workstation for cryogenic transmission electron microscopy according to an exemplary embodiment of the present invention will be described with reference to the accompanying drawings.

10 FIG. 2 is a cross-sectional view illustrating a workstation 100 for cryogenic transmission electron microscopy according to an exemplary embodiment of the present invention. As illustrated in FIG. 2, the workstation 100 for cryogenic transmission electron
15 microscopy of the present invention generally includes a stand 101, an insulated vessel 102, a Dewar vessel 103, and a holder 5.

The stand 101 has the shape of a plate, upper and lower surfaces of which are flat, and functions as a base
20 on which the insulated vessel 102 and the Dewar vessel 103 are disposed.

The insulated vessel 102 is disposed on one side of the upper surface of the stand 101, and is provided with a holder insertion socket 106 on a sidewall thereof. A
25 transparent cover 107 has a liquid nitrogen injection port

109 and a sample loading port 108, and is detachably mounted on an upper end of the insulated vessel 102. Here, the transparent cover 107 is provided with a step 107' on the outer circumference of an upper surface thereof. A
5 space is formed at the upper portion of the transparent cover 107 by the step 107'. Nitrogen gas, formed by evaporation and discharge of the liquid nitrogen in the insulated vessel 102, is confined in a space of the upper portion of the transparent cover 107. The nitrogen gas
10 thus confined serves as a boundary layer for preventing moisture in the air from becoming frozen on the upper surface of the transparent cover 107. In this manner, since no freezing phenomenon occurs on the upper surface of the transparent cover 107, a worker can rapidly load a
15 biological sample onto the holder 105 without damage and in a state in which the worker ensures a clear field of vision. The transparent cover is preferably made of acryl. Besides acryl material, any plastic material will do as long as it can be used at low temperature.

20 The Dewar vessel 103 is disposed on the other side of the stand 101 so as to face the holder insertion socket 106, and is provided with a charging port (not shown) capable of charging liquid nitrogen and a cap 104 capable of opening and closing the charging port at an upper end
25 thereof. The Dewar vessel 103 is provided with a holder

coupling hole 111 in a sidewall thereof which faces the insulated vessel 102. The liquid nitrogen charged in the Dewar vessel 103 cools the holder 105 fitted into the holder coupling hole 111.

5 The holder 105 onto which the biological sample is loaded is coupled to the holder insertion socket 106 and the holder coupling hole 111 at opposite ends thereof, wherein the end of the holder 105 onto which the biological sample is loaded is inserted into the holder insertion
10 socket 106. The first end of the holder 105 inserted into the holder insertion socket 106 is provided with an O-ring 112 made of rubber material in order to maintain airtightness on an outer circumference thereof.

Further, the workstation for cryogenic transmission
15 electron microscopy according to an exemplary embodiment of the present invention further includes a height adjuster 110 on a lower surface of the stand 101 on which the Dewar vessel 103 is disposed. The height adjuster 110 functions to incline the stand 101 such that the height at which the
20 Dewar vessel 103 is installed is higher than that at which the insulated vessel 102 is installed. When the height adjuster 103 inclines the stand 101 such that the height of the Dewar vessel 103 is higher than that of the insulated vessel 102, the liquid nitrogen can be prevented from
25 coming into direct contact with the O-ring 112 interposed

between the first end of the holder 105 and the holder insertion socket 106, and blocks of ice generated by mixture of moisture and liquid nitrogen in the insulated vessel 102 in the process of charging the liquid nitrogen into the insulated vessel 102 can be collected on the side opposite the sample because of the inclination of the stand, and thus the sample can be prevented from contamination.

Particularly, as illustrated in FIG. 3, the height adjuster 110 includes two short rods 110', each of which has a regular hexagonal cross section, and a long rod 110'', which connects the two short rods 110' at a position deviating from the center of the regular hexagonal cross section of each short rod 110' in a direction perpendicular to one of six sides of the regular hexagonal cross section of each short rod 110' and has a circular cross section. The lower surface of the stand 101 is supported in contact with the long rod 110'' alone. Since the long rod 110'' deviates from the center of the regular hexagonal cross section of each short rod 110', the height of the long rod 110'' can be adjusted in four steps. Among the six sides of the regular hexagonal cross-sectional short rod 110', four sides have not the same center, which make it possible to perform the height adjustment in four steps by rotating the two short rods 110'. FIG. 3 illustrates the case in which

the long rod 110" is highest from the ground. The height adjuster can be made of aluminum.

A process of loading a frozen biological sample onto the holder 105 using the workstation for cryogenic
5 transmission electron microscopy according to an exemplary embodiment of the present invention will be described below.

First, the opposite ends of the holder 105 are coupled to the holder insertion socket 106 and the holder coupling
10 hole 111 of the work station 100, respectively. At this time, the first end of the holder 105, onto which the biological sample is loaded, is inserted into the holder insertion socket 106.

Next, the height adjuster 110 is installed on the
15 lower surface of the stand 101 on which the Dewar vessel 103 is disposed. The inclination of the stand 101 is properly adjusted using the height adjuster 110 which is capable of performing a four-step height adjustment process.

20 When overall setting of the workstation 100 is completed though the aforementioned processes, liquid nitrogen is charged through the liquid nitrogen injection port 109 of the insulated vessel 102. Further, liquid nitrogen is charged through the charging inlet (not shown)
25 opened by taking off the cap 104 of the Dewar vessel 103.

When the entire workstation 100 is maintained under low temperature during this process, the sample is loaded onto the first end of the holder 105 through the sample loading port 108 of the insulated vessel 102 using
5 tweezers. At this time, the liquid nitrogen continues to be injected into the insulated vessel 102 so as to keep it under low temperature conditions. When the loading of the sample is completed, the holder 105 is separated from the workstation, and then is transferred to a transmission
10 electron microscope.

As described above, the workstation for cryogenic transmission electron microscopy has been described through the exemplary embodiment of the present invention. However, it will be understood that the embodiments are
15 illustrative and that the invention scope is not so limited. Any variations, modifications, additions, and improvements to the embodiment described are possible. These variations, modifications, additions, and improvements may fall within the scope of the inventions as
20 detailed within the following claims.

【Industrial Applicability】

According to the embodiment of the present invention, the workstation for cryogenic transmission electron microscopy, which observes the biological sample at low
25 temperature using the transmission electron microscope or

HVEM, can more rapidly and efficiently load the biological sample, processed at low temperature, on the holder of the workstation, and thus is useful for the cryogenic testing in which it is important to maintain a low temperature.

【CLAIMS】**【Claim 1】**

A workstation for cryogenic transmission electron microscopy, comprising:

5 a stand, upper and lower surfaces of which are flat;

an insulated vessel disposed on one side of the upper surface of the stand, and including a holder insertion socket on a sidewall thereof, wherein a transparent cover having a liquid nitrogen injection port and a sample
10 loading port is detachably mounted on an upper end of the insulated vessel, and includes a step on an outer circumference of an upper surface thereof;

a Dewar vessel disposed on another side of the upper surface of the stand so as to face the holder insertion
15 socket, including a charging port for charging liquid nitrogen and a cap for opening and closing the charging port at an upper end thereof, and having a holder coupling hole in a sidewall thereof which faces the insulated vessel; and

20 a holder, opposite ends of which are coupled to the holder insertion socket and the holder coupling hole.

【Claim 2】

The workstation as set forth in claim 1, wherein the transparent cover is made of acryl.

25 **【Claim 3】**

The workstation as set forth in claim 1, further comprising a height adjuster, which is disposed on the lower surface of the stand on which the Dewar vessel is disposed, and inclines the stand such that a height at
5 which the Dewar vessel is installed is higher than that at which the insulated vessel is installed.

【Claim 4】

The workstation as set forth in claim 3, wherein the height adjuster includes two short rods, each of which has
10 a regular hexagonal cross section, and a long rod connecting the two short rods and having a circular cross section, the long rod being connected at a position deviating from a center of the regular hexagonal cross section of each short rod in a direction perpendicular to
15 one of six sides of the regular hexagonal cross section of each short rod, and the lower surface of the stand is in contact with the long rod.

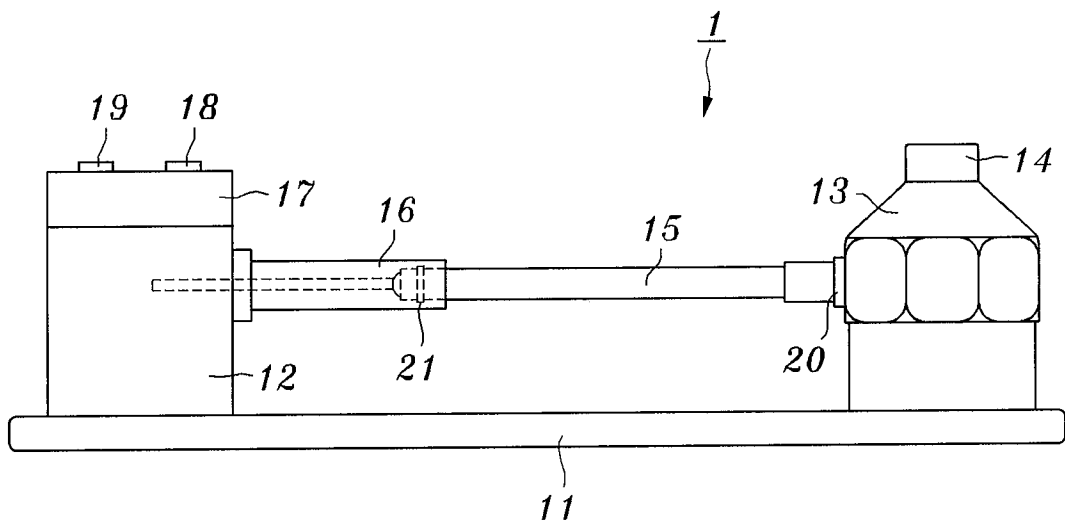
【Claim 5】

The workstation as set forth in claim 4, wherein the
20 height adjuster is made of aluminum.

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Figures

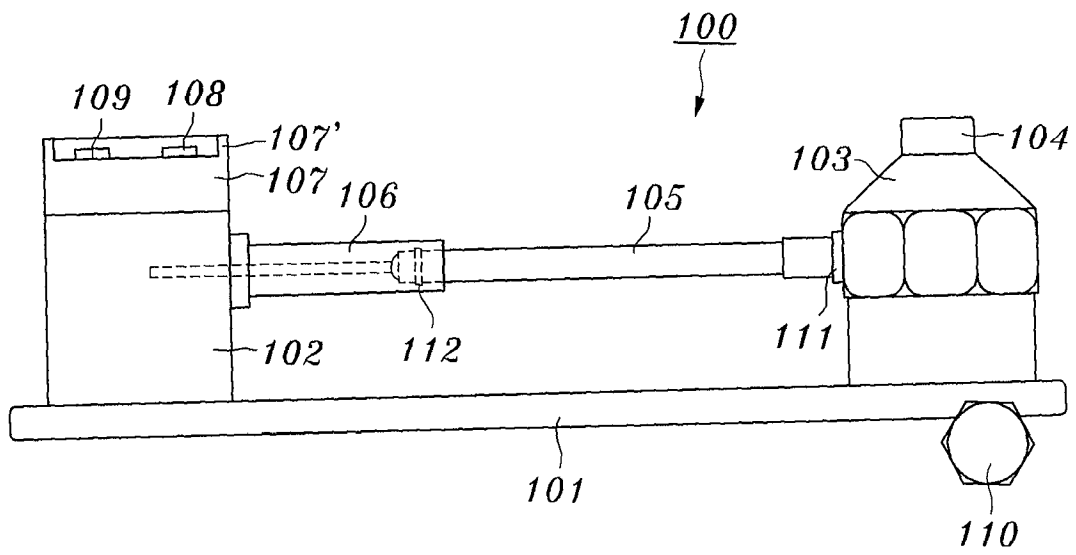
Fig. 1



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Figures

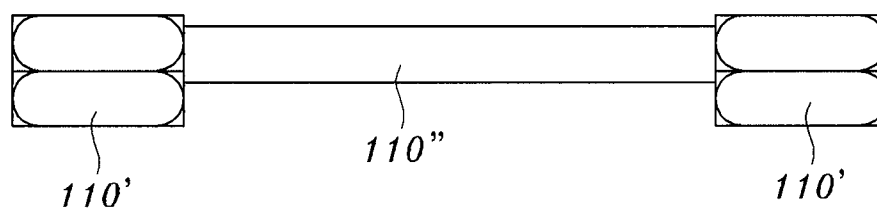
Fig. 2



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Figures

Fig. 3



A. CLASSIFICATION OF SUBJECT MATTER**G01N 1/28(2006.01)i**

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 H01J 37/20, H01J 37/20, G01N1/42, G01N 1/28 , G01N 23/22 , G01N 23/225 , H01J 37/20

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

Korean utility models and applications for utility models since 1975

Japanese utility models and applications for utility models since 1975

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

eKIPASS (KIPO internal) "cryo", "transmission", "electron", "microscope", "holder"

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 06410925 B1 (ARMBRUSTER, BARBARA L. et al.) 25 JUNE 2002 see the whole document	1-5
A	EP 01852889 A2 (FEI COMPANY) 07 NOVEMBER 2007 see thw whole document	1-5
A	WO 2002077612 A1 (UNIVERSITEIT MAASTRICHT) 03 OCTOBER 2002 see the whole document	1-5
A	JP 2005-158288 A (CANON KK) 16 JUNE 2005 see the whole document	1-5



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

18 DECEMBER 2008 (18.12.2008)

Date of mailing of the international search report

18 DECEMBER 2008 (18.12.2008)

Name and mailing address of the ISA/KR

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/KR2008/003061

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6410925 B1	25.06.2002	DE 60102593 D1 EP 1305814 B1 JP 2004-508661 JP 2004-508661 T US 6410925 B1 WO 02-11174 A1	06.05.2004 31.03.2004 18.03.2004 18.03.2004 25.06.2002 07.02.2002
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