

(12) STANDARD PATENT
(19) AUSTRALIAN PATENT OFFICE

(11) Application No. **AU 2011303063 B2**

(54) Title
Administration apparatus, operating method thereof and administration method

(51) International Patent Classification(s)
A61M 5/00 (2006.01)

(21) Application No: **2011303063** (22) Date of Filing: **2011.09.08**

(87) WIPO No: **WO12/036226**

(30) Priority Data

(31) Number	(32) Date	(33) Country
2010-205881	2010.09.14	JP

(43) Publication Date: **2012.03.22**

(44) Accepted Journal Date: **2014.06.05**

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(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
22 March 2012 (22.03.2012)

(10) International Publication Number
WO 2012/036226 A1

(51) International Patent Classification:
A61M 5/00 (2006.01)

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(21) International Application Number:

PCT/JP2011/071058

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(22) International Filing Date:

8 September 2011 (08.09.2011)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

2010-205881 14 September 2010 (14.09.2010) JP

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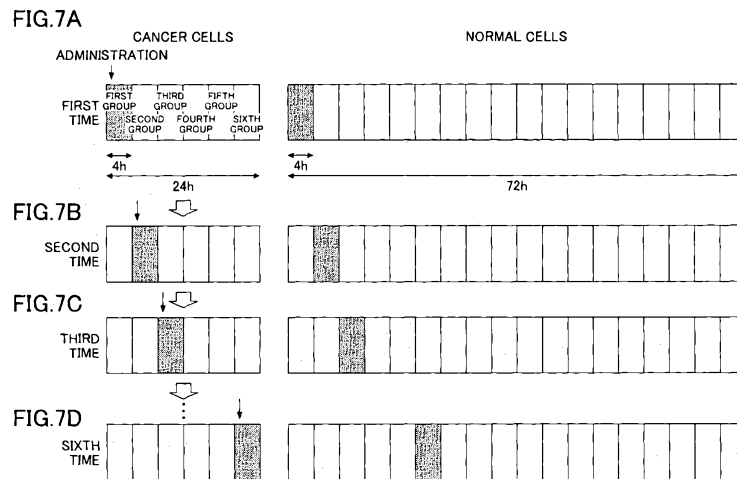
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(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: ADMINISTRATION APPARATUS, OPERATING METHOD THEREOF AND ADMINISTRATION METHOD



(57) Abstract: An administration apparatus to administer an inhibitor drug to a patient to inhibit cell division of a malignant cell includes an administration unit configured to administer the inhibitor drug to the patient; an administration timing storage unit configured to store an administration time to start an administration of the inhibitor drug; a time measurement unit configured to measure a current time; and a control unit configured to drive and control the administration unit so as to administer the inhibitor drug to the patient when the current time coincides with the administration time. The administration time is set on a basis of a pre-determined phase of a cell cycle of the malignant cell.

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DESCRIPTION

TITLE OF THE INVENTION

ADMINISTRATION APPARATUS, OPERATING METHOD
5 THEREOF AND ADMINISTRATION METHOD

TECHNICAL FIELD

The present invention generally relates to
administration apparatuses, operating methods thereof
10 and administration methods. More specifically, the
present invention relates to an administration
apparatus, an operating method thereof and an
administration method to administer an inhibitor drug
that inhibits cell division of a malignant cell to a
15 patient.

BACKGROUND ART

Each document, reference, patent application
or patent cited in this text is expressly
20 incorporated herein in their entirety by reference,
which means that it should be read and considered by
the reader as part of this text. That the document,
reference, patent application or patent cited in this
text is not repeated in this text is merely for
25 reasons of conciseness.

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The following discussion of the background to the invention is intended to facilitate an understanding of the present invention only. It should be appreciated that the discussion is not an acknowledgement or admission that any of the material referred to was published, known or part of the common general knowledge of the person skilled in the art in any jurisdiction as at the priority date of the invention.

10 FIGS. 1 through 5 show conventional typical administration methods and efficacy rates of anticancer drugs. FIG. 1 is a table showing conventional administration methods and efficacy rates of methotrexate. FIG. 2 is a table showing 15 conventional administration methods 5-fluorouracil. FIG. 3 is a table showing a randomized trial result of various treatments that have been conventionally practiced in Japan, Europe and the United States. FIG. 4 is a table showing conventional administration 20 methods of vincristine. FIG. 5 is a table showing remission rates for various malignant tumors in conventional administration methods.

All administration methods shown in FIGS. 1 through 5 are methods that perform injections or drip 25 injections, take drug holidays for weeks until a side

effect of administrations disappears, and repeat the administrations (see, for example, Non-patent Document 1 and Non-patent Document 2).

5 However, the conventional administration methods shown in FIGS. 1 through 5 have had a problem of anticancer drugs not being able to exert their effectiveness sufficiently because drug solutions are administrated at arbitrary timing without respect to a cell cycle of a cancer cell. This regard is
10 discussed in detail below with reference to accompanying drawings.

FIG. 6 is a diagram showing an example of a cell cycle. The cell cycle is a concept of viewing a process where the cells divide and the number of
15 cells doubles as a single cycle. The cell cycle is formed of a cycle composed of respective phases including a DNA synthesis preparation phase (i.e., nymphochrysalis: G1 phase), a DNA synthesis phase (S phase), a cell division preparation phase
20 (imagochrysalis: G2 phase), and a cell division phase (M phase). Here, cells that temporarily or reversibly stop the cell division are regarded to be in a stationary phase called G0 phase. A single cancer cell doubles by completing the cell cycle, and
25 continues to doubly increase. The anticancer drug is

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a generic name of a medical drug, agent or substance that has a function of inhibiting proliferation of the cancer cells, and is roughly divided into two kinds, a time-dependent type drug and a
5 concentration-dependent type drug. The time-dependent type drug shows its effectiveness related to the cell cycle.

It is thought that the time-dependent type anticancer drug effectively acts on G1 phase of the
10 cell cycle shown in FIG. 6, and shows the effectiveness by putting a brake on the progress. The cancer is composed of many cancer cells, and the respective cancer cells are in different phases of the cell cycle. Therefore, even if the anticancer
15 drug is administered in certain timing, the effectiveness of the anticancer drug can be obtained only to the cancer cells in G1 phase at the administered timing, and the anticancer drug cannot produce the effect on the cells in the other phases.

20 Here, if the cell cycle of the cancer cells is made T , and a period of G1 phase where the anticancer drug can produce the effect is made t , when the anticancer drug at first is administered in a certain timing, a ratio of the number of cells that
25 the anticancer drug can prevent the cell division is

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t / T to all cells, and a rate of the number of cells that escape from the effect is $(T - t) / T$ to all cells. If the conventional administration methods are repeated n times (where n is an integer), a ratio
5 of the number of cells that escape from the effect after n times is $((T - t) / T)^n$.

As an example, if the cell cycle T is made 24h; G1 phase t is made 4h; and the number of administration is made six times, it is found that
10 $(20 / 24)^6 = 0.3349 = 33.5\%$ of the cancer cells remain.

That means that the conventional administration methods have a problem of not being able to exclude the cancer cells that escape from the inhibitory effect in theory, even if the frequency of
15 administration is increased.

Furthermore, because a continuous administration time is long, there is a problem of a physical and mental strain of a patient who receives a dose being great. More specifically, since a small
20 amount of anticancer drug is diluted with a solution, and a treatment is carried out by giving the patient a drip continuously for a long time, the patient comes to take large volumes of fluid. Because of this, the patient has to go to a restroom frequently,
25 which causes a large burden to the patient. Moreover,

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because the conventional administration methods
impose on the kidneys of the patient, there has been
a problem of not being able to perform the
administration to the patient having a kidney
5 disorder. In addition, if the administration is
performed by hospital visit, the best timing can be
midnight, depending on the administration timing. In
this case, there has been a problem of the
administration being a burden for both of a
10 healthcare professional and the patient.

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>

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SUMMARY OF INVENTION

Accordingly, embodiments of the present
invention may provide an administration apparatus, an
operating method thereof and an administration method
25 solving one or more of the problems discussed above

to at least some extent, or at least provide the consumer with a useful or commercial choice.

According to a broad aspect of the present invention, there is provided an administration apparatus to administer an inhibitor drug to a patient to inhibit cell division of a malignant cell including:

an administration unit configured to administer the inhibitor drug to the patient;

an administration timing storage unit configured to store an administration time to start an administration of the inhibitor drug;

a time measurement unit configured to measure a current time; and

a control unit configured to drive and control the administration unit so as to administer the inhibitor drug to the patient when the current time coincides with the administration time,

wherein the administration time is set on a basis of a predetermined phase of a cell cycle of the malignant cell.

Preferably, a phase when a cell division inhibition effect by the inhibitor drug is the highest is selected as the predetermined phase in the cell cycle;

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the cell cycle is divided into a plurality of groups by a predetermined period not more than a duration time of the predetermined phase; and

the administration time is set plural times
5 at not less than $(T + t)$ intervals if the cell cycle is made T , and the predetermined period is made t , and is set so that a difference of respective administration times for the plurality of groups is less than a two cycle period.

10 Preferably, the predetermined period is set at the duration time of the predetermined phase.

Preferably, the administration apparatus further comprises:

an administration period storage unit to
15 store an administration period to administer the inhibitor drug continuously,

wherein the administration period is set at not more than the duration time of the predetermined phase.

20 Preferably, the administration time is set so that intervals before and after the administration time equal $(AT + t)$ if A is made a constant of a natural number.

25 Preferably, the administration apparatus

further comprises:

an administration rate storage unit to store an administration rate to administer the inhibitor drug; and

5 a medication information input unit to allow medication information to be input,

wherein a dosage is input and set through the medication information input unit, and a pair of continuing administration and non-administration is made a basic cycle based on the dosage, the administration time, the administration period, and the administration rate; and

10 wherein a whole control including a number of the units needed to administer the dosage to the patient, and the control unit perform the whole control automatically.

Preferably, the administration time is set at a number not less than the number of the plural groups.

20 Preferably, the malignant cell is a cancer cell; and

the inhibitor drug is a anticancer drug.

Preferably, the inhibitor drug is a drug solution; and

25 the administration unit administers the

drug solution by transfusion to a blood circulating system in the patient's body.

Preferably, the administration unit includes a transfusion pump.

5 Preferably, the administration unit includes a blocking unit to block a channel for the transfusion during the non-administration.

10 Preferably, the administration unit includes a flow sensor in the channel for the transfusion, and

the control unit performs a feedback control so as to make a flow rate of the drug solution constant, based on a flow rate value detected by the flow rate sensor.

15 Preferably, the administration apparatus further comprises:

a blocking warning unit to warn that the channel for the drug solution is blocked,

20 wherein the control unit blocks the channel for the drug solution by the blocking unit, and warns that the channel for the drug solution is blocked by driving the blocking warning unit if the flow rate value detected by the flow rate sensor is over a predetermined standard value.

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According to another broad aspect of the present invention, there is provided an operating method of an administration apparatus, the administration apparatus including,

5 an administration unit configured to administer an inhibitor drug to a patient to inhibit cell division of a malignant cell;

an administration timing storage unit configured to store an administration time at which to start an administration of the inhibitor drug;

10 a time measurement unit configured to measure a current time;

an administration period storage unit to store an administration period of administering the inhibitor drug continuously to the patient; and

15 a control unit configured to drive and control the administration unit so as to administer the inhibitor drug to the patient when the current time coincides with the administration time,

20 the operating method including the steps of:

setting the administration time and the administration period on a basis of a predetermined phase of the cell division of the malignant cell;

25 storing the set administration time in the

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administration time storage unit and the set administration period in the administration period storage unit respectively; and

5 administering the inhibitor drug to the patient continuously for the administration period when the current time measured by the time measurement unit coincides with the administration time by controlling the administration unit with the control unit.

10 According to another broad aspect of the present invention, there is provided an administration method to administer an inhibitor drug to a patient to inhibit cell division of a malignant cell, including the steps of:

15 setting an administration time to start an administration of the inhibitor drug to the patient on a basis of a predetermined phase of the cell division of the malignant cell;

20 storing the set administration time in an administration time storage unit; and

administering the inhibitor drug to the patient continuously when the current time coincides with the administration time stored in the administration storage unit.

25

According to a further broad aspect of the present invention, there is provided an administration apparatus to administer an inhibitor drug to a patient to inhibit cell division of a malignant cell comprising:

an administration unit configured to administer the inhibitor drug to the patient;

an administration timing storage unit configured to store an administration time to start an administration of the inhibitor drug;

a time measurement unit configured to measure a current time; and

a control unit configured to drive and control the administration unit so as to administer the inhibitor drug to the patient when the current time coincides with the administration time;

wherein the administration time is set on a basis of a predetermined phase of a cell cycle of the malignant cell;

wherein a phase when a cell division inhibition effect by the inhibitor drug is the highest is selected as the predetermined phase in the cell cycle;

the cell cycle is divided into a plurality of groups by a predetermined period not more than a

duration time of the predetermined phase; and

the administration time is set plural times
at not less than $(T + t)$ intervals if the cell cycle
is made T , and the predetermined period is made t ,
5 and is set so that a difference of respective
administration times for the plurality of groups is
less than a two cycle period.

According to another broad aspect of the
present invention, there is provided an operating
10 method of an administration apparatus, the
administration apparatus including,

an administration unit configured to
administer an inhibitor drug to a patient to inhibit
cell division of a malignant cell;

15 an administration timing storage unit
configured to store an administration time at which
to start an administration of the inhibitor drug;

a time measurement unit configured to
measure a current time;

20 an administration period storage unit to
store an administration period of administering the
inhibitor drug continuously to the patient; and

a control unit configured to drive and
control the administration unit so as to administer
25 the inhibitor drug to the patient when the current

time coincides with the administration time,
the operating method comprising the steps
of:

5 setting the administration time and the
administration period on a basis of a predetermined
phase of a cell cycle of the malignant cell, wherein
a phase when a cell division inhibition effect by the
inhibitor drug is the highest is selected as the
predetermined phase in the cell cycle, the cell cycle
10 is divided into a plurality of groups by a
predetermined period not more than a duration time of
the predetermined phase, and the administration time
is set plural times at not less than $(T + t)$
intervals if the cell cycle is made T , and the
15 predetermined period is made t , and is set so that a
difference of respective administration times for the
plurality of groups is less than a two cycle period;
 storing the set administration time in the
administration time storage unit and the set
20 administration period in the administration period
storage unit respectively; and
 administering the inhibitor drug to the
patient continuously for the administration period
when the current time measured by the time
25 measurement unit coincides with the administration

time by controlling the administration unit with the control unit.

According to another broad aspect of the present invention, there is provided an
5 administration method to administer an inhibitor drug to a patient to inhibit cell division of a malignant cell, comprising the steps of:

setting an administration time to start an administration of the inhibitor drug to the patient
10 on a basis of a predetermined phase of a cell cycle of the malignant cell, wherein a phase when a cell division inhibition effect by the inhibitor drug is the highest is selected as the predetermined phase in the cell cycle, the cell cycle is divided into a
15 plurality of groups by a predetermined period not more than a duration time of the predetermined phase, and the administration time is set plural times at not less than $(T + t)$ intervals if the cell cycle is made T , and the predetermined period is made t , and
20 is set so that a difference of respective administration times for the plurality of groups is less than a two cycle period;

storing the set administration time in an administration time storage unit; and
25 administering the inhibitor drug to the

patient continuously when the current time coincides with the administration time stored in the administration storage unit.

5 BRIEF DESCRIPTION OF THE DRAWINGS

In order that the invention may be more fully understood and put into practice, preferred embodiments thereof will now be described with reference to the accompanying drawings in which:

10 FIG. 1 is a table showing conventional administration methods and efficacy rates of methotrexate;

FIG. 2 is a table showing conventional administration methods for 5-fluorouracil;

15 FIG. 3 is a table showing a randomized trial result of various treatments that have been conventionally practiced in Japan, Europe and the United States;

20 FIG. 4 is a table showing conventional administration methods of vincristine;

FIG. 5 is a table showing remission rates for various malignant tumors in conventional administration methods;

25 FIG. 6 is a diagram showing an example of a cell cycle;

FIG. 7A is a diagram showing an example of a first administration of an administration method of a first embodiment;

FIG. 7B is a diagram showing an example of a

second administration of the administration method of the first embodiment;

FIG. 7C is a diagram showing an example of a third administration of the administration method of the first embodiment;

FIG. 7D is a diagram showing an example of a sixth administration of the administration method of the first embodiment;

FIG. 8 is a diagram showing an example of a configuration of an administration apparatus of the first embodiment;

FIG. 9 is a diagram showing an example of a state of having a patient wear the administration apparatus of the first embodiment;

FIG. 10 is a diagram showing an internal configuration of an example of a controller of the administration apparatus of the first embodiment;

FIG. 11 is an example of a processing flow of an operating method of an administration apparatus and an administration method using the administration apparatus of the first embodiment;

FIG. 12 is a diagram showing an example of a configuration of an administration apparatus of a second embodiment;

FIG. 13 is a diagram showing an example of a

configuration of an administration apparatus of a third embodiment;

FIG. 14A is a diagram showing an example of a first administration of an operating method of an administration apparatus and an administration method of a fourth embodiment;

FIG. 14B is a diagram showing an example of a second administration of the operating method of the administration apparatus and the administration method of the fourth embodiment;

FIG. 14C is a diagram showing an example of a third administration of the administration method of the fourth embodiment;

FIG. 14D is a diagram showing an example of a fourth administration of the operating method of the administration apparatus and the administration method of the fourth embodiment;

FIG. 14E is a diagram showing an example of a sixth administration of the operating method of the administration apparatus and the administration method of the fourth embodiment;

FIG. 15A is a diagram showing an example of a first administration of an operating method of an administration apparatus and an administration method of a fifth embodiment;

FIG. 15B is a diagram showing an example of a second administration of the operating method of the administration apparatus and the administration method of the fifth embodiment;

5 FIG. 15C is a diagram showing an example of a third administration of the operating method of the administration apparatus and the administration method of the fifth embodiment; and

10 FIG. 15D is a diagram showing an example of a sixth administration of the operating method of the administration apparatus and the administration method of the fifth embodiment.

DESCRIPTION OF EMBODIMENTS

15 A description is given below, with reference to accompanying drawings of embodiments of the present invention.

20 FIG. 6 is a diagram showing an example of a cell cycle. As mentioned above, the cell cycle is a concept of viewing a process where cells divide and the number of cells doubles as a single cycle. The cell cycle is formed of a cycle composed of respective phases of a DNA synthesis preparation phase (i.e., nymphochrysalis: G1 phase), a DNA
25 synthesis phase (S phase), a cell division

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preparation phase (imagochrysalis: G2 phase), and a cell division phase (M phase). A cancer cell becomes two cancer cells by going round the cell cycle once, the number of the cells continues to double. An anticancer drug is a generic name of a medical drug, agent or substance that has a function of inhibiting proliferation of the cancer cells, and roughly divided into two kinds of drugs, a time-dependent type drug and a concentration-dependent type drug. The time-dependent type drug shows its effect related to the cell cycle. A phase that shows the effect of inhibiting proliferation of the cancer cell is made a predetermined phase.

It is thought that the time-dependent type anticancer drug acts effectively on the G1 phase of the cell cycle shown in FIG. 6, and shows its effect by putting a brake on the progress. Because the cancer is composed of many cancer cells, and respective cancer cells are in different phases in the cell cycle, the anticancer drug that works on the G1 phase shows a more highly effect by a long time administration. As typical time-dependent type anticancer drugs, 5-fluorouracil, methotrexate, vincristine and the like are cited as examples.

Here, a concentration-dependent type drug

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has a character that increases cell killing effectiveness as a dosage amount increases (concentration dependency), and massive dose is performed just the same.

5 On the other hand, the anticancer drug has a function that inhibits the cell division, or harms the cells directly, and naturally causes damage even to normal cells. More specifically, the anticancer drug may cause damage to a bone marrow where cell
10 proliferation is active (where a blood cell is created), an alimentary canal mucosa, and a liver or a kidney that has functions of decomposing a drug and carrying the drug out of the body. The more the anticancer drug is used, the more a side effect is
15 caused. Therefore, it is necessary to use the anticancer drug, considering a balance between the effect and the side effect of the anticancer drug.

 In the cell cycle shown in FIG. 6, if the anticancer drug effectively acts on the G1 phase, by
20 administering the anticancer drug to each cancer cell only in the G1 phase, the anticancer drug can be administered most effectively, and the side effect on the normal cells can be reduced.

 However, in reality, the plural cancer cells
25 exist in the patient's body, and the respective

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cancer cells advance the respective cell cycles in different timings. Accordingly, all of the cancer cells do not enter the G1 phase together in the same timing, but the respective cancer cells enter the G1
5 phase in different timings. Because of this, in the conventional anticancer drug administration methods, there have been no other methods than administering the anticancer drug in an arbitrary timing by ignoring the cell cycle, or administering the
10 anticancer drug diluted to a low concentration into the patient's body for a long time. Due to this, the anticancer drug has not been able to produce the cell division inhibition effect sufficiently, and the burden on the patient and the healthcare professional
15 has been great in the event of the long time continuous administration.

[First Embodiment]

FIGS. 7A through 7D are diagrams to illustrate a basic principle of an administration
20 method of a first embodiment. FIG. 7A is a diagram showing an example of a first administration of an administration method of a first embodiment in comparison to an effect to normal cells. Similarly, FIG. 7B shows a second administration of the
25 administration method of the first embodiment; FIG.

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7C is shows a third administration of the
administration method of the first embodiment; and
FIG. 7D shows a sixth administration of the
administration method of the first embodiment in
5 comparison to the effect to normal cells respectively.

In FIGS. 7A through 7D, as an example, a
cell cycle of cancer cells is made 24 hours (24h),
and a time length (or a time period) of G1 phase
where an anticancer drug functions is made four hours
10 (4h). Also, a cell cycle of normal cells is made 72
hours (72h).

In this case, as shown in FIG. 7A, if the
time length of the G1 phase (4h) is made a standard,
and the cell cycle (24h) is divided by the time
15 length of the G1 phase as a basic unit, the cell
cycle can be divided into $24 / 4 = 6$ groups. All of
the cancer cells enter the G1 phase at any timing in
the six groups. Here, the G1 phase of the respective
cancer cells do not always start and finish at the
20 same timings as the six groups' start and end, but
spread over two groups in many cases, which has no
problem, though. This point is described hereinafter.

At the first administration timing, the
cells in a period when the anticancer drug works
25 exist in a $4 / 24 = 1 / 6$ probability. If this is

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called a first group, the anticancer drug works on
the cancer cell in the first group. In the first
anticancer drug administration, the anticancer drug
is continuously administered for a predetermined
5 period in four hours of the time length of the G1
phase, and the administration is stopped. The
administration period varies according to the
anticancer drug. For example, the administration
period may be a several minutes or may be a few hours
10 within four hours.

As shown in FIG. 7B, after the first
administration, the administration is stopped, and a
second administration is performed. At this time, if
the second administration timing is made 24 hours
15 after the start of the first administration, which is
the same as the cycle time, because the anticancer
drug is administered only to the cancer cell in the
first group, and have the effect of the cancer
inhibition only on the cancer cells in the first
20 group, there is only a small inhibition effect on the
whole cancer cells. Accordingly, the second
administration is, for example, performed 28 hours
after the start of the first administration, by which
the administration timing is adjusted so as to take
25 effect on the cancer cells in the second group. By

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doing this, the anticancer drug can exert the effect on the cancer cells in both of the first and second groups. At this time, the anticancer drug is administered to the cancer cells that enter the G1 phase at timing that spreads over the first group and the second group so as to cover the entire G1 phase, and the anticancer drug can be administered to the cancer cells uniformly.

Next, as shown in FIG. 7C, in a third administration, the anticancer drug is administered so that the anticancer drug exerts effectively on the cancer cells in the third group. That means that the administration is performed 28 hours after the second administration. In addition, the administration period may be the same as the period of the first time and the second time, or may be different from the period of the first time and the second time according to a property and the like of the anticancer drug.

Though not shown in FIGS. 7A through 7D, by repeating fourth and fifth administrations every 28 hours for 4 hours period intermittently in a way similar to the second and third times, the anticancer drug can be administered to the cancer cells that enter the G1 phase in the fourth and fifth groups so

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that the anticancer drug can effectively work on the cancer cells in the fourth and fifth groups.

As shown in FIG. 7D, if the sixth administration is performed another 28 hours after the fifth administration, the cell division inhibition effect of the anticancer drug can be provided for the all cancer cells. Though the anticancer drug also affects the normal cells, as shown in the right side of FIGS. 7A through 7D, because a cell cycle of the normal cells is 72 hours, a single administration affects only $4 / 72 = 1 / 18$ of the all normal cells, and even the all six-time administrations affect only $24 / 72 = 1 / 3$ of the all normal cells.

In this way, by dividing a cell cycle into plural groups on a basis of a predetermined time (or a predetermined period) where an anticancer drug can act effectively on cancer cells, by intermittently administering the anticancer drug to the divided plural groups on the basis of the predetermined time in sequence, by finally administering the anticancer drug to all the groups, and by providing the anticancer drug for the entire cell cycle, the anticancer drug can be administered effectively to the cancer cells, reducing an adverse effect on the

normal cells.

Here, in the present embodiment, the cell cycle of the malignant cells are divided by using the continuous period of the G1 phase where the anticancer drug inhibits the proliferation of the malignant cells as a basic unit, but it is possible to make the basic unit for division a shorter period than that of the G1 phase. Even in this case, by intermittent and comprehensive administrations, the anticancer drug can be administered to all the malignant cells at the G1 phase timing, reducing the effect on the normal cells.

However, if the divided period is shorter than the G1 phase, fear of performing an overlapping administration to the same malignant cells increases. In other words, when the administration period is quite short, and the administration is viewed as a point in terms of time, as the example described in FIGS. 7A through 7D, if the basic unit for division is the same as the G1 phase, the malignant cells' reception of the administration of the anticancer drug is only one time in one cycle administration for all the malignant cells. If one cycle of the malignant cells is expressed as a circle; six equally divided points on the circumference of the circle are

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expressed as administration timings; the circle and points are made a first circle (which corresponds to setting the administration time of the present embodiment); a second circle that has the same size
5 as the first circle is provided; $1 / 6$ of the circumference of the second circle is shown as the G1 phase; the second circle is superposed on the first circuit; and the second circle is rotated on the first circle (which corresponds to various malignant
10 cells advancing the cell cycle in an arbitrary cycle), it is found that the second circle includes only one administration among the six-time administrations of the first circle. In other words, if the basic unit of the divided period is made equal to the period of
15 the G1 phase, in the one cycle administration, the G1 phase corresponds to the administration timing only one time with respect to all of the malignant cells. Hence, it is possible to administer the inhibitor drug at the G1 phase uniformly to all of the
20 malignant cells.

On the other hand, if the divided period of the respective groups is set shorter than the G1 phase, since the G1 phase of the malignant cells may include twice administrations at the beginning and
25 the end of the G1 phase, even in the administration

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for one cycle, some malignant cells will receive
twice administrations of the anticancer drug while
other malignant cells will receive one-time
administration of the anticancer drug, which may not
5 be a completely averaged administration.

Furthermore, if the divided period is made
longer than the period of the G1 phase, because there
may be malignant cells whose G1 phase is included in
an interval between the administrations, the
10 malignant cells that are not administered in the G1
phase may occur.

In addition, in the administration method of
the first embodiment, if the administration period
has a certain amount of duration, there may be
15 malignant cells that receive one-time administration
of the anticancer drug in the G1 phase and malignant
cells that receive double administrations of the
anticancer drug in the G1 phase. However, in the
event that the divided period is the same as the G1
20 phase, even if the administration of the G1 phase
spans across the two groups, the total anticancer
administered time length in a cycle equals among all
of the malignant cells, and the anticancer drug can
be administered to all the malignant cells in a
25 uniform dosage even in this case.

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Therefore, it is possible to make the basic unit for division slightly shorter or longer than the period of G1 phase, which is still expected to be able to obtain a more sufficient effect than the conventional administration method. However, in order to perform a more effective and uniform administration of the anticancer drug, it is preferable to divide the cell cycle by a duration time of a predetermined phase where the anticancer drug acts most effectively as a basic unit, and to set plural groups.

As described above, in the administration apparatus, operating method thereof and administration method of the present embodiment, specified administration apparatus, operating method thereof and administration method are realized by basing on such a view of administering the anticancer drug on the basis of the predetermined period of the cell cycle.

Here, in FIG. 7, the G1 phase is described to be a phase where the anticancer drug acts effectively. However, since another phase of the cell cycle can be a phase where the anticancer drug works effectively, depending on a combination between the cells and the drug, in that case, another phase

of the cell cycle may be a standard.

Hereinafter, a more detailed description is given about specific configuration examples of the administration apparatus, operating method thereof
5 and administration method of the present embodiment. Heretofore, an example of the malignant cell to be necrotized being the cancer cell, and the drug to be used being the anticancer drug is cited. However, because the administration apparatus, operating
10 method thereof and administration method of the present invention can be used for a general malignant cell or tumor that performs cell division, the drug can be generalized and called an inhibitor drug or an inhibitor.

15 FIG. 8 is a diagram showing a configuration of an example of an administration apparatus of a first embodiment of the present invention. In FIG. 8, the administration apparatus of the first embodiment includes a controller 40, a transfusion pump 50, a
20 transfusion blocking mechanism 60, a transfusion tube 70, a needle 71, and a drug solution container (which may be called a drug solution bag) 72. The needle 71 is provided at an end of the transfusion tube 70, and the transfusion pump 50 and the transfusion blocking
25 mechanism 60 are provided in the middle of the drug

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solution tube 70. The controller 40 is electrically connected to the transfusion pump 50 and the transfusion blocking mechanism 60. For example, the transfusion pump 50, transfusion tube 70, needle 71 and drug solution container 72 may be provided as a transfusion set of a set of assembly.

The administration apparatus of the present embodiment is explained as an administration unit that administers an inhibitor drug into a patient's body, by citing a unit that uses the transfusion pump 50 as an example. If the administration to the patient is performed by using the transfusion pump 50, a drug solution of liquid is used as a drug, and the administration is performed by administering the drug solution into a vein in the patient's body by transfusion. The principle of the administration method of the first embodiment described in FIG. 7 can be applied to general inhibitor drugs that inhibit cell division of malignant cells without limiting the drug solution, and various administration units appropriate for the administered inhibitor drug can be used. However, to make the explanation easy, the description is given about the administration apparatus using the transfusion hereinafter. However, the administration

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apparatus, operating method thereof and administration method of the present invention can be applied to various cases of administrating the inhibitor drug that inhibits the cell division of the malignant cells to the patient, and can be used for other intramuscular administration, subcutaneous administration, dermal administration, transnasal administration, parenteral administration such as lung administration, or oral administration and the like. Therefore, the administration apparatus, the operating method thereof and the administration method are not limited to those by transfusion.

The transfusion pump 50 is a transfusion unit to transport the inhibitor drug (i.e., drug solution) contained in the drug solution container 72 through the transfusion tube 70 in a direction toward the needle 71 at the end. Various transfusion pumps 50 are available, as long as the transfusion pump 50 can transport the drug solution.

The transfusion blocking mechanism 60 is a unit to block the transfusion when the drug solution is not administered. The transfusion blocking mechanism 60 may be, for example, a mechanism that clogs a flow channel and blocks the transfusion by pressing the transfusion tube 70 and by compressing

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the transfusion tube 70 from the outside. In this case, with regard to the method of compressing the transfusion tube 70, for example, a method of compressing the transfusion tube 70 directly by
5 mobile arm driven by a motor, a compressing method by screw and the like can be used according to intended purpose.

The controller 40 is provided as a unit that controls the drive of the transfusion pump 50 and the
10 drive of the transfusion blocking mechanism 60.

FIG. 9 is a diagram showing an example of a state of having a patient wear the administration apparatus of the first embodiment. The controller 40 is worn around the body of patient. Moreover, the
15 drug solution container 72 that is not shown in FIG. 9 is built into a case 73. The transfusion pump 50 is provided near the case 73 and connected to the drug solution container 72 by the transfusion tube 70, and they are worn around the patient's body in an
20 integrated manner. The transfusion blocking mechanism 60 is worn close to the body of patient as well as the transfusion pump 50. The inhibitor drug transported by the transfusion pump 50 is pumped into the patient's body through the transfusion tube 70
25 and the needle 71.

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FIG. 10 is a diagram showing an example of an internal configuration of the controller 40 of the first embodiment. In FIG. 10, the controller 40 of the first embodiment includes a medication
5 information input unit 10, an administration timing storage unit 11, an administration period storage unit 12, an administration rate storage unit 13, an time measurement unit 14, a control unit 15, a transfusion pump drive unit 16, and a transfusion
10 blocking mechanism drive unit 17. Moreover, in FIG. 10, a transfusion pump 50 and a transfusion blocking mechanism 60 connected to the controller 40 are shown as outside components.

The medication information input unit 10 is
15 an input unit to allow a healthcare professional to set an administration timing of the inhibitor drug (e.g., time to start the administration such as at what time?; i.e., what o'clock and minutes), a duration time of the administration and, an
20 administration rate (e.g., as measured in ml per hour). In other words, the controller 40 is configured so that the healthcare professional can set an injecting time interval and an injection dose of the inhibitor drug, that is, a transfusion period
25 and a transfusion rate, depending on the type of

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inhibitor drug.

Here, the medication information input unit 10 may be configured to allow the healthcare professional to input other related information such as a type of the inhibitor drug and a dosage, and the input information may be determined depending on the intended use. The medication information input unit 10 may be configured to be a selection-type input device such as a touch panel, or may be configured to be an input device into which a setting number is directly input, item by item. The medication information input unit 10 can adopt various configurations and input methods depending on the intended use.

The administration timing storage unit 11 is a unit to store an administration time to start the administration input that is input and set at the medication information input unit 10. Similarly, the administration period storage unit 12 is a unit to store the administration period that is input and set at the medication information input unit 10, and the administration rate storage unit 13 is a unit to store the administration rate that is input and set at the medication information input unit 10. The administration timing storage unit 11, the

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administration period storage unit 12 and the administration rate storage unit 13 may be configured, for example, to be a rewritable nonvolatile memory such as a flash memory and the like.

5 The time measurement unit 14 is a unit to measure a current time, and a general timer and the like may be used. In the administration apparatus of the present embodiment, because the set administration time is stored in the administration storage unit 11, whether the current time becomes the administration time can be determined depending on whether the time output from the time measurement unit 14 coincides with the administration time stored in the administration storage unit 11.

15 The transfusion pump drive unit 16 is a unit to drive the transfusion pump 50. The transfusion pump drive unit 16 may be connected to the transfusion pump 50 and the control unit 15, and may be configured to drive the transfusion pump 50, according to an instruction of the control unit 15.

20 The transfusion blocking mechanism drive unit 17 is a drive unit to drive or stop the transfusion blocking mechanism 60 according to the instruction from the control unit 15, and is connected to the control unit 15 and the transfusion

25

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blocking unit 17. More specifically, the transfusion
blocking mechanism drive unit 17 turns the
transfusion blocking mechanism 60 off when the
transfusion is performed, and turns the transfusion
5 blocking mechanism 60 on when the transfusion is not
performed, according to the instruction of the
control unit 15. This makes it possible to certainly
stop the drug solution provision when the drug
solution is not administered.

10 The control unit 15 is a unit to control the
transfusion pump drive unit 16 and the transfusion
blocking mechanism drive unit 17, and to administer
or not to administer the drug solution at a
predetermined timing. The control unit 15 is
15 connected to the transfusion pump drive unit 16 and
the transfusion blocking mechanism drive unit 17, and
drives the transfusion pump 50 and the transfusion
blocking mechanism 60 based on the information stored
in the administration timing storage unit 11, the
20 administration period storage unit 12 and the
administration rate storage unit 13.

More specifically, the time measurement unit
14 is connected to the control unit 15, and when the
time set in the administration timing storage unit 11
25 and the time output from the time measurement unit 14

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coincide, the control unit 15 makes the transfusion blocking mechanism drive unit 17 release the transfusion blocking mechanism 60, and makes the transfusion pump 50 start its operation. After that, 5 the control unit 15 makes the transfusion pump 50 carry out the transfusion at the transfusion rate stored in the administration rate storage unit 13, only for the predetermined period stored in the administration period storage unit 12. After the 10 time elapses the predetermined period, the control unit 15 makes the transfusion pump 50 stop the transfusion, and makes the transfusion blocking mechanism 60 active.

Moreover, the control unit 15 makes the 15 transfusion blocking mechanism drive unit 17 work if the control unit 15 does not make the transfusion pump 50 work, and performs the control to surely stop the administration of the drug solution. In other words, the release of the transfusion blocking 20 mechanism drive unit 17 is performed in accordance with the timing when the transfusion is carried out, and the transfusion is blocked again at the timing of the end of the transfusion by the control unit 15.

In this way, in the administration apparatus 25 of the present embodiment, the transfusion is blocked

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while the transfusion is not performed by the transfusion blocking mechanism 60 and the transfusion blocking mechanism drive unit 17. By doing this, it is possible to administer the inhibitor drug at a predetermined time interval at exact intervals, and intermittently, and to block the transfusion while the administration is not performed.

Here, the control unit 15, for example, may be configured to be a micro computer that includes a CPU and works by reading a program, or to be an electrical circuit that includes a predetermined operational circuit.

With this configuration, the administration apparatus, operating method thereof and administration method of the first embodiment, as described in FIG. 7, can practice the administration of the inhibitor drug at the timing when the inhibitor drug acts effectively on all of the malignant cells that advance the cell cycle at different timings, though the administration is intermittent. This allows a single administration period to be short, which can reduce the adverse effect on the normal cells, and makes it possible to administer the inhibitor drug to all of the malignant cells in full at the timing when the inhibitor drug

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exerts effectively on the overall malignant cells such as a malignant tumor and the like.

More specifically, if the administration apparatuses shown in FIGS. 8 through 10 are operated, and the administration method shown in FIG. 7 is practiced, a description is given as follows. Here, as preconditions, as shown in FIG. 7, for a malignant cell that has a 24-hour cell cycle and a 4-hour G1 phase, the 24-hour cell cycle is divided into 4-hour parts, and six groups are set.

If a healthcare professional sets and inputs a first administration time at 0:00 on day X, a second administration time at 4:00 on day (X+1) of 28 hours after the first administration time, a third administration time at 8:00 on day (X+2) of 28 hours after the second administration time, a fourth administration time at 12:00 on day (X+3) of 28 hours after the third administration time, a fifth administration time at 16:00 on day (X+4) of 28 hours after the fourth administration time, and a sixth administration time at 20:00 on day (X+5) of 28 hours after the fifth administration time into the medication information input unit 10, the administration times of respective times are set and stored in the administration timing storage unit 11.

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Also, if the healthcare professional sets an administration period at a predetermined period (for example, P hours) and inputs the predetermined period into the medication information input unit 10 at the same time, a duration time of the respective administration is set at P hours, and the administration period is set and stored to be P hours in the administration period storage unit 12. Similarly, if the healthcare professional sets an administration rate at Q ml / h and inputs the administration rate into the medication information input unit 10, the administration rate is set and stored to be Q ml / h in the administration rate storage unit 13.

In this manner, in a state of setting the administration time in the administration timing storage unit 11, the administration period in the administration period storage unit 12, and the administration rate in the administration rate storage unit 13, the administration starts. Then, each time the current time output from the time measurement unit 14 coincides with the six administration times set in the administration timing storage unit 11 at 28-hour intervals, the control unit 15 releases the drive of the transfusion

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blocking mechanism drive unit 17, drives transfusion
pump drive unit 16, and administers the inhibitor
drug to a patient by releasing a blocking state of
the transfusion blocking mechanism 60 and by driving
5 the transfusion pump 50. At this time, the
administration rate follows the Q ml / h set and
stored in the administration rate storage unit 13,
and with regard to the administration period, the
administration is continuously performed for P hours
10 that have been set and stored in the administration
period storage unit 12. After finishing the P -hour
continuous administration, the control unit 15
controls the transfusion pump drive unit 16 so as to
stop the transfusion pump 50, and controls the
15 transfusion blocking mechanism drive unit 17 so as to
drive the transfusion blocking mechanism 60.

By making the controller 40 execute such a
control, the administration apparatus of the present
embodiment carries out the administration of the
20 inhibitor drug to the patient in an administration
pattern shown in FIG. 7, by which the effect on the
normal cells can be reduced, and the inhibitor drug
is administered to all of the malignant cells at the
G1 phase where the administration is effective.

25 FIG. 11 is a diagram showing an example of

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an operating method of the administration apparatus
and an administration method using the administration
apparatus of the first embodiment. In FIG. 11, the
same numerals are used for the components similar to
5 those described hereinbefore, and the description is
omitted.

In FIG. 11, in step S100, the medication
information is input. A healthcare professional may
input the medication information including an
10 administration time, an administration period, and an
administration rate into the medication information
input unit 10.

At that time, the administration time is set
on a basis of a predetermined phase of a cell cycle
15 of the target malignant cells to inhibit the cell
division thereof. In the example described in FIGS.
6 and 7, the administration time is set on the basis
of the G1 phase. In other words, the timing when the
inhibitor drug is administered to the malignant cells
20 in the G1 phase is set. If some target malignant
cells to be necrotized by inhibiting the cell
division can be specified, an inhibitor drug may be
administered individually at timing when the phase of
the cell cycle of the target malignant cells becomes
25 the G1 phase. However, in general, since the

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malignant cells exist at a level where the number and
respective cell cycles cannot be specified, and the
cell cycles of the respective malignant cells advance
in different timings, it is difficult to administer
5 the inhibitor drug individually in the G1 phase to
all of the malignant cells. Therefore, an
administration pattern having administration timing
so as to administer all of the malignant cells in the
G1 phase without recognizing the cell cycles of the
10 malignant cells individually is established.

As an example, as described in FIG. 7,
plural groups are set by dividing the cell cycle by
the same period as the duration time of the G1 phase,
and the administration time and the administration
15 period are set so as to administer the inhibitor drug
to each group among the plural groups in sequence at
predetermined intervals. With respect to the
administration rate, if there is a value such as
default depending on the inhibitor drug type, the
20 default value may be adopted and set.

Here, in FIGS. 6 and 7, a description is
given by citing the example of the G1 phase being
effective as a period of administering the inhibitor
drug, but another period may be timing when the
25 inhibitor drug acts effectively depending on the

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5 patient's disease and a used inhibitor drug. In such a case, the administration timing may be determined on a basis of a period when an inhibition effect on cell division by the inhibitor drug functions most effectively.

10 In step S110, among the medication information input into the medication information input unit 10 by the healthcare professional, the administration time, the administration period and the administration rate are respectively stored in the administration timing storage unit 11, the administration period storage unit 12 and the administration rate storage unit 13, and the administration time, administration period and administration rate are set as information that the control unit 15 refers to.

20 In step S120, checking the current time with the set administration time is started. Measurement of the current time is performed by the time measurement unit 14. The control unit 15 starts checking and comparison between the current time input from the time measurement unit 14 and the administration time stored in the administration storage unit 11.

25 In step S130, it is determined whether the

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current time coincides with the administration time set in the administration timing storage unit 11. The determination is performed by the control unit 15 into which the output from the time measurement unit 5 14 is input and capable of referring to the administration time stored in the administration timing storage unit 11.

In step S130, if the control unit 15 determines that the current time coincides with the set administration time, the flow advances to step 10 S140. On the other hand, if the control unit 15 determines that the current time does not coincide with the set administration time, the flow enters a stand by state circulating step S130.

15 In step S140, if the current time is determined to coincide with the administration time in step S130, the administration of the inhibitor drug to the patient is carried out. The administration of the inhibitor drug is performed 20 according to the administration rate and the administration time previously set in steps S100 and S110. With this, the inhibitor drug can be administered at the effective timing to administer the inhibitor drug, and the effect of inhibiting the 25 cell division can be enhanced.

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In step S150, after starting the administration, if the administration reaches the set predetermined administration period, the administration is stopped. This allows the inhibitor drug to be administered to the patient only in the predetermined amount in a single administration, which makes it possible to inhibit an adverse effect on the normal cells, and to administer the inhibitor drug effectively.

10 In step S160, the control unit 15 determines whether the current time goes by all of the administration times set in the administration timing storage unit 11. If the current time has already elapsed the set administration time, this means that all the set administrations have been finished, so the processing flow in FIG. 11 is finished. On the other hand, if the administration time that has not been passed is still set in the administration timing storage unit 11, the flow returns to step S130, enters a standby state that determines whether the current time coincides with the administration time, and enters a state of waiting for the current time passing the remaining administration time.

25 Then, in the end, if the inhibitor drug is administered at all of the set administration time,

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the flow in FIG. 13 is finished.

Here, in the administration apparatus in the first embodiment, it is also possible to set the transfusion timing, changing the transfusion time intervals depending on the patient's conditions, different from the regular administration setting shown in FIG. 7, by setting and storing arbitrary plural times of information in the administration timing storage unit 11. For example, if a first administration time is made at 0:00 of Y day; a second administration time is made at 2:00 of (Y+1) day; and a third administration time is made at 6:00 of (Y+2) day, a time interval between the first and second administration and a time interval between the second and third administration can be individually set. Besides, elapsed time from the first administration may be directly set such as the second administration being 26 hours later and the third administration being 28 hours later. Also, values set in the administration time storage unit 12 and the administration rate storage unit 14 can be individually set depending on the number of the transfusion (administration). This means that varying the first drug solution amount and the second drug solution amount is possible.

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In this manner, according to the administration apparatus, operating method thereof and administration method of the first embodiment, an inhibitor drug can be administered to malignant cells
5 in a predetermined phase in a cell cycle at timing when cell division inhibition effectiveness of the inhibitor drug can acts most efficiently, and only the exact necessary amount of inhibitor drug can be administered corresponding to the cell cycle of the
10 target cells. If such an administration method of the inhibitor drug of the cell division is possible, because the inhibitor drug is not needed to be administered with much for long time as the conventional administration method, the physical
15 strain of the patient can be reduced, and an effective treatment can be performed. Also, the patient does not need to go to a restroom frequently.

Moreover, by performing infusion of the inhibitor drug intermittently plural times, the
20 administration of inhibitor drug of the cell division can be carried out most effectively corresponding to the cell cycle of the target cells. If the explanation is given in the example shown in FIG. 7, by performing the second administration 24 hours + 4
25 hours = 28 hours after the first administration,

providing the effect for another group of cancer cells is possible. After that, it is possible to repeat the administration every 28 hours, or to change the time intervals depending on the patient's
5 conditions and hospital visit schedule. In short, it is possible to administer the anticancer drug most efficiently and effectively, considering a time ratio between the cell cycle of the cancer cells and a period that the anticancer drug can act effectively,
10 and to reduce strains of both of the patient and healthcare professional.

[Second Embodiment]

FIG. 12 is a diagram showing a configuration of an example of an administration apparatus of a
15 second embodiment of the present invention. The administration apparatus of the second embodiment is similar to the configuration of the administration apparatus of the first embodiment in that a controller 41 includes a medication information input
20 unit 10, an administration timing storage unit 11, an administration time storage unit 13, a time measurement unit 14, a control unit 15, a transfusion pump drive unit 16, and a transfusion blocking mechanism drive unit 17, and further include a
25 transfusion pump 50 and a transfusion blocking

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mechanism 60. The same numerals are put to components similar to the components described in the first embodiment, and the explanation is omitted.

On the other hand, the administration apparatus of the second embodiment differs in that the controller 40 further include a drug information input unit 20, a drug information storage unit 21 and a medication information calculation unit 22 inside.

The drug information input unit 20 is an input unit that allows a healthcare professional to input drug information to be administered. The drug information input unit 20 is, for example, configured to be sufficient to work if only information to specify the drug such as a type of drug and the like is input.

The drug information storage unit 21 is a database that stores optimum administration information such as administration timing, a dosage and the like for each drug. If the drug is a type of drug that is administered by transfusion, the drug information storage unit 21 stores drug solution information such as transfusion timing, a transfusion amount and the like.

The transfusion information calculation unit 22 is a unit that refers to the drug information

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stored in the drug information storage unit 21 based
on the drug information input into the drug
information input unit 20, calculates an optimum
administration information for the input drug, and
5 sets respective administration information of the
administration time, administration period and
administration rate in the administration timing
storage unit 11, administration period storage unit
12 and administration rate storage unit 13. This
10 allows the healthcare professional to not need to
search and set the optimum drug administration
conditions individually, to automatically set a
specific operating method of the administration
apparatus and administration method by only inputting
15 the information to specify the drug such as type of
the drug and the like into the drug information input
unit 20, and to reduce his or her strain.

Here, if the optimum administration amount
is determined by the drug type, by determining the
20 administration time, administration period and
administration rate, when a continuous pair of the
administration and non-administration is made a basic
cycle, the whole cycle number needed to administer
the optimum administration amount is determined.
25 This means that the entire schedule such as period

necessary for the whole administration, and the strain of the healthcare professional can be substantially reduced.

Here, the administration apparatus of the
5 second embodiment also includes the medication information input unit 10. In other words, the administration apparatus of the second embodiment is configured to be able to change the administration timing, administration amount, administration rate
10 and the like, by using the medication information input unit 10. This allows the healthcare professional to set a part of the medication information manually and the medication information calculation unit 22 and the like to set the remaining
15 item automatically. For example, it is possible to adopt a using method of setting the administration rate and administration period by the medication information calculation unit 22, and setting only the administration timing by manual using the medication
20 information input unit 10.

Thus, according to the administration apparatus, operating method thereof and administration method, time intervals that administer the inhibitor drug, an amount of the inhibitor drug
25 to be administered, a type of the inhibitor drug, and

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the other settings related to the administration of
the inhibitor drug are automatically practiced by
being preliminarily set. Because of this, even if
the administration time is midnight, the healthcare
5 professional such as a doctor or a nurse do not need
to bear a burden with respect to the administration
directly. In addition, for a patient, a hospital
admission is not a necessary condition for a
treatment, because the inhibitor drug is
10 automatically administered at necessary timing for
the treatment for 24 hours. Moreover, in the case of
hospital admission, if the administration time comes
in midnight, since the administration is performed
automatically, the patient can receive the
15 administration in a stable state. Furthermore,
because the treatment can be continued in home
healthcare, the patient can be released from the
economic stress and the stress of hospitalization.

In this way, according to the administration
20 apparatus, operating method thereof and
administration method, by increasing a degree of
automatic setting of the administration setting, the
strain of the healthcare professional and the patient
can be substantially reduced, and the administration
25 of the inhibitor drug can be performed effectively,

reducing the adverse effect on the normal cells.

[Third Embodiment]

FIG. 13 is a diagram showing a configuration of an example of an administration apparatus of a third embodiment of the present invention. In FIG. 13, the administration apparatus of the third embodiment is common to the administration apparatus of the first embodiment in that the administration apparatus includes a medication information input unit 10, an administration timing storage unit 11, an administration period storage unit 12, an administration rate storage unit 13, a time measurement unit 14, a control unit 15, a transfusion pump drive unit 16, and a transfusion blocking mechanism drive unit 17 inside the controller 42, and a transfusion pump 50 and a transfusion blocking mechanism 60 outside the controller 42. Here, the same numerals are used for components similar to those in the first embodiment, and the description is omitted.

In the meanwhile, the administration apparatus of the third embodiment differs from the administration apparatus of the first embodiment in that a transfusion rate comparison unit 31 is provided inside a control unit 15 in the controller

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42, and a transfusion rate detection unit 30 is provided inside the transfusion pump 50. Also, the administration apparatus of the third embodiment may include a blocking warning unit 61 outside the
5 controller 42.

The transfusion rate detection unit 30 is a unit to detect a transfusion rate in the transfusion pump 50 or the transfusion tube 70. For example, a flow sensor and the like may be used for the
10 transfusion rate detection unit 30. The transfusion rate detection unit 30 is provided inside the transfusion pump 50 or in the neighboring transfusion tube 70. FIG. 13 shows an example of providing the transfusion rate detection unit 30 inside the
15 transfusion pump 50.

The transfusion rate comparison unit 31 is a unit that compares an actual transfusion rate inside the transfusion pump 50 or the neighboring transfusion tube 70 with an administration rate (i.e.,
20 transfusion rate) set in the administration rate storage unit 13. For example, a comparator and the like may be used for the transfusion rate comparison unit 31.

The blocking warning unit 61 is a unit to
25 warn outward that the channel for the drug solution

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is blocked if the actual transfusion rate is over a predetermined standard transfusion rate.

In FIG. 13, an output of the transfusion rate detection unit 30 is compared with an output of the administration rate storage unit 13 by the transfusion rate comparison unit 31, and the control unit 15 controls the transfusion pump drive unit 16 based on the comparison result. With this, a feedback control is performed so that the amount of drug injected into the patient's body per unit time constantly agrees with the value set in the administration rate storage unit 13.

In this manner, in the administration apparatus of the third embodiment, the transfusion rate detection unit 30 detects the actual transfusion rate in real time, and the transfusion rate is controlled by the feedback control based on the detection value. Because of this, since the transfusion rate is controlled so as to be constantly the same as the value set in the administration rate storage unit 13, even if there is disturbance such as a back pressure change from the body, a gravity change due to a height difference between the needle 71 and the drug solution bag 72 and the like, a transfusion of a constant flow rate can be accurately

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performed by canceling the effect. This makes it possible to realize a stable treatment even if the inhibitor drug has the effect in a very small amount, to put it the other way around, even if the inhibitor drug needs to be strictly managed about the dosage.

Moreover, in the transfusion rate detection unit 30, should the flow rate over the predetermined set value be detected, the transfusion rate comparison unit 31 detects the abnormal transfusion rate. At this time, the control unit 15 immediately controls the transfusion blocking mechanism drive unit 17, and a control that stops the transfusion may be performed. Also, the controller 42 may drive the blocking warning unit 61 so as to warn outside people that the channel for the drug solution is blocked. This makes it possible to safely prevent the flow rate over the regulated amount from being administrated into the body.

Here, the contents described in the first embodiment can be directly applied to the operating method of the administration apparatus and administration method using the same of the third embodiment. Because the transfusion rate can be more accurately managed in the operating method of the administration apparatus and the administration

method than those in the first embodiment, the inhibitor drug can be administered more accurately in the third embodiment than the first embodiment.

[Fourth Embodiment]

5 FIGS. 14A through 14E are diagrams to illustrate an operating method of an administration apparatus and an administration method of a fourth embodiment of the present invention. The operating method of the administration apparatus and the
10 administration method of the fourth embodiment can be commonly performed in the administration apparatus of the first through third embodiments, the operating method of the administration apparatus and the
15 administration method of the fourth embodiment are described without particularly distinguishing the first through third embodiments.

 The administration method described in FIG. 7 in the first embodiment is a method of dividing the 24-hour cell cycle by 4-hour G1 phase into six groups,
20 and administering the inhibitor drug in sequence at 28-hour intervals for the first through sixth groups.

 However, for the first through sixth groups, it is not necessary to administer the inhibitor drug, and it is possible to administer the inhibitor drug
25 every other group. Moreover, it is not necessary to

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perform administration every cell cycle, but is possible to perform administration at plural cycle intervals such as every two cycle or every three cycles. In the operating method of the administration apparatus and the administration method of the fourth embodiment, a description is given about such an administration method. Here, in FIG. 14, with respect to the cell cycle, administration period and divided group number, similar to FIG. 7, the description is given by citing an example of the cell cycle being made 24 hours, the administration period being made 4 hours, and the divided group number being made six.

FIG. 14A is a diagram showing an example of a first administration of the administration method of the fourth embodiment. In the first administration, an inhibitor drug is administered to the first group.

FIG. 14B is a diagram showing an example of a second administration of the administration method of the fourth embodiment. In FIG. 14B, in the second administration, the inhibitor drug is administered to the third group. At this time, the administration time is 56 hours after the first administration. In other words, from the first administration time, two-

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cycle interval longer than the one cycle is taken, and by further adding the time intervals of the first group and the second group, the inhibitor drug is administered to the third group.

5 FIG. 14C is a diagram showing an example of a third administration method of the fourth embodiment. In the third administration, the inhibitor drug is administered to the fifth group. In this case also, a 56-hour interval is taken for
10 the second administration time.

 FIG. 14D is a diagram showing an example of a fourth administration of the administration method of the fourth embodiment. In the fourth administration, the inhibitor drug is administered to
15 the second group. A 36-hour interval is taken from the third administration time. The interval is shorter than 48 hours corresponding to a two-cycle period, but longer than 24 hours corresponding to a one-cycle period, so the administration is performed
20 at a sufficient time interval.

 FIG. 14E is a diagram showing an example of a sixth administration of the administration method of the fourth embodiment. Here, though a fifth administration is not shown in FIGS. 14E and 14E, the
25 fifth administration is performed to the fourth group

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by taking a 32-hour interval for the fourth
administration, and the sixth administration in FIG.
14E is carried out to the sixth group. In this case
also, a 32-hour interval is taken from the fifth
5 administration.

In this manner, it is not always to
administer the inhibitor drug to the divided groups
in sequence, if the administration intervals are
sufficiently taken, the administration is executed in
10 arbitrary order to the divided groups. In addition,
the longer the administration intervals, the smaller
the effect provided for the normal cells by the
administration. Accordingly, the intervals of the
plural cycles may be taken longer than the one-cycle
15 period. Though the whole administration requires a
long period, since the accumulative administration
period is short, considering a patient's sufficient
restoration of strength, the inhibitor drug can be
administered to each group effectively, without
20 affecting the normal cells in an adverse way. Here,
in the fourth embodiment, the administration to the
normal cells can be limited to $24 / 72 = 1 / 3$.

In addition, in the fourth embodiment, the
description is given by citing the example of
25 administering the inhibitor drug to every other group,

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but the administration may be performed at $(nT + t)$ intervals in the administration method in the first embodiment. Here, "T" is a cell cycle of a malignant cell; "t" is a duration time of a predetermined
5 period of performing the administration; and "n" is a natural number not less than two.

As described in the first embodiment and the fourth embodiment, if the time intervals before and after the administration time is set to have time
10 intervals not less than at least a one-cycle period, intervals such that the normal cells do not receive the effect by the administration can be sufficiently provided between the successive administrations. Moreover, by performing the administration in
15 sequence by making the divided group a target, the administration can be carried out to all the malignant cells in full at timing when the inhibitor drug can act effectively.

Thus, by making an intermittent
20 administration pattern that does not occur a continuous administration for a long period of time, diluting the concentration of the drug solution is not necessary, and performing the administration at an appropriate concentration that has a sufficient
25 effect on inhibition of cell division of the

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malignant cells is possible. By removing the
necessity of diluting the concentration, the whole
dosage can be reduced, and the frequency of the
urination of the patient can be reduced, which makes
5 it possible to reduce strain on a patient.

Here, as described in the first and fourth
embodiment, with respect to the administration order
of the inhibitor drug to the plural groups, various
orders of the administration patterns can be
10 considered, but the administration pattern such that
a difference of the number of administrations among
the groups is not more than once may be adopted. By
performing such an administration, a simultaneous
occurrence of a group to which any inhibitor drug is
15 not administered and a group to which the inhibitor
drug is administered not less than twice can be
removed. In other words, if there is a group that
has received an administration one extra time, the
administration to the group can be stopped until the
20 other group receives the same times of administration
as the group, the inhibitor drug can be administered
so as to be uniform to all of the groups. This
administration method can be applied not only to the
case of the administration for only a one-cycle
25 period of the cell cycle, but also to the case of the

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administration for cycles across not less than a two-
cycle period. This means that the second-round
administrations are not started before the first-
round administrations are not performed to all the
5 groups, and the next round administrations can be
started after finishing respective round
administrations.

Furthermore, the number of administration of
the inhibitor drug is preferably set at the number
10 equal to or more than the plural groups, and the not
less than once administration is preferably performed,
in terms of administering the inhibitor drug to all
the malignant cells at the G1 phase at least once.

In this manner, according to the
15 administration method of the fourth embodiment, it is
possible to reduce the adverse effect on the normal
cells and to inhibit the cell division of the
malignant cells effectively, using the various
administration patterns.

20 [Fifth Embodiment]

FIGS. 15A through 15D are diagrams showing
an example of an operating method of an
administration apparatus and an administration method
of a fifth embodiment of the present invention. FIG.
25 15A is a diagram showing an example of a first

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administration of the operating method of the administration apparatus and the administration method of the fifth embodiment. FIG. 15B is a diagram showing an example of a second administration
5 of the operating method of the administration apparatus and the administration method of the fifth embodiment. FIG. 15C is a diagram showing an example of a third administration of the operating method of the administration apparatus and the administration
10 method of the fifth embodiment. FIG. 15D is a diagram showing an example of a sixth administration of the operating method of the administration apparatus and the administration method of the fifth embodiment.

15 The operating method of the administration apparatus and the administration method of the fifth embodiment differ from the administration method in FIG. 7 of the first embodiment in that a cell cycle of a malignant cell is 22 hours. The operating
20 method of the administration apparatus and the administration method of the fifth embodiment are similar to the administration method in FIG. 7 in that a duration time of the G1 phase of the cell cycle of the malignant cell is four hours and the
25 cell cycle is divided into six groups. The other

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preconditions are made similar to the administration method in FIG. 7. Here, the cell cycle becomes shortened to 22 hours, by which the number of the malignant cells in the G1 phase in the sixth group is
5 thought to be about a half of the number of the malignant cells in the G1 phase of the other groups. The operating method of the administration apparatus and the administration method of the fifth embodiment differ from the administration method in FIG. 7 of
10 the first embodiment in that the sixth group is made like a fraction to the other groups.

Here, since the operating method of the administration apparatus and the administration method of the fifth embodiment can be practiced in
15 the administration apparatuses of the first through third embodiments, a description is given without particular limitations.

As shown in FIG. 15A, in a first administration, the inhibitor drug is administered to
20 the malignant cells of a first group in the G1 phase at first administration timing as a target. The inhibitor drug effectively exerts the cell division inhibition effect on the malignant cells in the first group that enter the G1 phase at the first
25 administration timing.

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As shown in FIG. 15B, in a second administration, the inhibitor drug is administered to the malignant cells of a second group in the G1 phase at second administration timing as a target, at 26
5 hours after the first administration time. The inhibitor drug produces the cell division inhibition effect on the malignant cells in the second group that enter the G1 phase at the second administration timing.

10 As shown in FIG. 15C, in a third administration, the inhibitor drug is administered to the malignant cells of a third group in the G1 phase at third administration timing as a target, at 26
15 hours after the second administration time. The inhibitor drug effectively exerts the cell division inhibition effect on the malignant cells in the third group that enter the G1 phase at the third administration timing.

20 After that, similar administrations are repeated as a fourth and a fifth administrations.

As shown in FIG. 15D, in a sixth administration, the inhibitor drug is administered to a sixth group 26 hours after the fifth administration time. Four hours are allotted to the first though
25 sixth groups, but a half of only two hours are

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allotted to the sixth group. Hence, the number of
the malignant cells that enters the G1 phase included
in the sixth group is about a half of the number of
the malignant cells that enters the G1 phase included
5 in the respective first through fifth groups. In
this case, for example, the sixth administration
period may be a half of the respective first through
fifth administration periods, and the dosage of the
inhibitor drug to the malignant cells belonging to
10 the sixth group (i.e., being in the sixth group at
the sixth administration timing) may be a half of the
dosage to the malignant cells belonging to the
respective first through fifth groups. This makes it
possible to administer the inhibitor drug to the
15 malignant cells in the first through sixth groups
uniformly. Thus, if the cell cycle is divided by a
duration time of a predetermined phase where the
inhibitor acts effectively, the cell cycle cannot be
divided into all equal parts, and a fraction can
20 occur. Even in this case, by regarding the broken
number as a single independent group, and for the
broken number of group, by setting an administration
period (i.e., dosage) corresponding to the group
length or the number of the malignant cells included
25 in the group, the administration methods described in

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the first and the fourth embodiments can be directly applied.

In this case, the effect that the inhibitor drug provide for the normal cells is $22 / 72 = 11 / 36 < 1 / 3$, and can be smaller than the case of the first and fourth embodiments.

Here, in the fifth embodiment, the sixth group of the last broken number is treated as the independent group, but by adding the broken number group to the fifth group, the administration period to the fifth group may be lengthened corresponding to the length of the broken number. In this case, the administrations are finished at five times to all of the plural groups of one cell cycle.

In this way, the group division method may base the duration time of the predetermined phase as a basic unit, but if the broken number occurs, by treating the group of the broken number as an individual group and by shortening the administration period to the group, the entire dosage can be adjusted. Or, by adding the group of the broken number to the other group and by lengthening the administration period to the group, the entire dosage can be adjusted. By doing this, an appropriate administration can be performed.

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Here, if the intermittent administration of the inhibitor drug is carried out for plural cycles over one cycle of the cell cycle, the broken number may be ignored and the administration of the
5 inhibitor drug may be performed making all the group an equal time length. In the second cycle, though the divided place of the group is different from the first cycle, since the cell cycle is properly divided into plural groups in the respective cycles, by
10 executing the administration on the basis of the group, the administration can be performed so as to reduce the effect on the normal cells, and so as to work the inhibitor drug effectively, similarly to the other embodiments.

15 According to an administration apparatus, an operating method thereof, and an administration method of one embodiment, cell division of a malignant cell can be effectively inhibited, and an adverse effect on a normal cell can be reduced.

20 The embodiments of the present invention can be applied to an administration apparatus, an operating method thereof and an administration method that use various administration units such as a transfusion pump and the like.

25 The present invention is not limited to

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these embodiments, but variations and modifications may be made without departing from the scope of the present invention.

The present application is based on
5 Japanese Priority Patent Application No. 2010-205881, filed on September 14, 2010, the entire contents of which are incorporated herein by reference.

Throughout the specification, unless the context requires otherwise, the word "comprise" or
10 variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers.

Furthermore, throughout the specification,
15 unless the context requires otherwise, the word "include" or variations such as "includes" or "including", will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group
20 of integers.

Modifications and variations such as would be apparent to a skilled addressee are deemed to be within the scope of the present invention.

25

CLAIMS

1. An administration apparatus to administer an inhibitor drug to a patient to inhibit cell division of a malignant cell comprising:

5 an administration unit configured to administer the inhibitor drug to the patient;

an administration timing storage unit configured to store an administration time to start an administration of the inhibitor drug;

10 a time measurement unit configured to measure a current time; and

a control unit configured to drive and control the administration unit so as to administer the inhibitor drug to the patient when the current
15 time coincides with the administration time;

wherein the administration time is set on a basis of a predetermined phase of a cell cycle of the malignant cell;

20 wherein a phase when a cell division inhibition effect by the inhibitor drug is the highest is selected as the predetermined phase in the cell cycle;

the cell cycle is divided into a plurality of groups by a predetermined period not more than a
25 duration time of the predetermined phase; and

the administration time is set plural times
at not less than $(T + t)$ intervals if the cell cycle
is made T , and the predetermined period is made t ,
and is set so that a difference of respective
5 administration times for the plurality of groups is
less than a two cycle period.

2. The administration apparatus as claimed
in claim 1,
10 wherein the predetermined period is set at
the duration time of the predetermined phase.

3. The administration apparatus as claimed
in claim 2, further comprising:
15 an administration period storage unit to
store an administration period to administer the
inhibitor drug continuously,
wherein the administration period is set at
not more than the duration time of the predetermined
20 phase.

4. The administration apparatus as claimed
in claim 3,
wherein the administration time is set so
25 that intervals before and after the administration

time equal $(AT + t)$ if A is made a constant of a natural number.

5 5. The administration apparatus as claimed in claim 3 or 4, further comprising:

an administration rate storage unit to store an administration rate to administer the inhibitor drug; and

10 a medication information input unit to allow medication information to be input,

wherein a dosage is input and set through the medication information input unit, and a pair of continuing administration and non-administration is made a basic cycle based on the dosage, the 15 administration time, the administration period, and the administration rate; and

20 wherein a whole control including a number of the units needed to administer the dosage to the patient, and the control unit perform the whole control automatically.

6. The administration apparatus as claimed in any one of the preceeding claims,

25 wherein the administration time is set at a number not less than the number of the plural groups.

7. The administration apparatus as claimed
in any one of the preceding claims,
wherein the malignant cell is a cancer
5 cell; and
the inhibitor drug is a anticancer drug.

8. The administration apparatus as claimed
in any one of the preceding claims,
10 wherein the inhibitor drug is a drug
solution; and
the administration unit administers the
drug solution by transfusion to a blood circulating
system in the patient's body.

15
9. The administration apparatus as claimed
in claim 8,
wherein the administration unit includes a
transfusion pump.

20
10. The administration apparatus as
claimed in claim 8 or 9,
wherein the administration unit includes a
blocking unit to block a channel for the transfusion
25 during the non-administration.

11. The administration apparatus as claimed in claim 10,

5 wherein the administration unit includes a flow sensor in the channel for the transfusion, and the control unit performs a feedback control so as to make a flow rate of the drug solution constant, based on a flow rate value detected by the flow rate sensor.

10

12. The administration apparatus as claimed in claim 11, further comprising:

a blocking warning unit to warn that the channel for the drug solution is blocked,

15

wherein the control unit blocks the channel for the drug solution by the blocking unit, and warns that the channel for the drug solution is blocked by driving the blocking warning unit if the flow rate value detected by the flow rate sensor is over a

20

predetermined standard value.

13. An operating method of an administration apparatus, the administration apparatus including,

25

an administration unit configured to

administer an inhibitor drug to a patient to inhibit cell division of a malignant cell;

an administration timing storage unit configured to store an administration time at which
5 to start an administration of the inhibitor drug;

a time measurement unit configured to measure a current time;

an administration period storage unit to store an administration period of administering the
10 inhibitor drug continuously to the patient; and

a control unit configured to drive and control the administration unit so as to administer the inhibitor drug to the patient when the current time coincides with the administration time,

15 the operating method comprising the steps of:

setting the administration time and the administration period on a basis of a predetermined phase of a cell cycle of the malignant cell, wherein
20 a phase when a cell division inhibition effect by the inhibitor drug is the highest is selected as the predetermined phase in the cell cycle, the cell cycle is divided into a plurality of groups by a predetermined period not more than a duration time of
25 the predetermined phase, and the administration time

is set plural times at not less than $(T + t)$ intervals if the cell cycle is made T , and the predetermined period is made t , and is set so that a difference of respective administration times for the plurality of groups is less than a two cycle period;

5 storing the set administration time in the administration time storage unit and the set administration period in the administration period storage unit respectively; and

10 administering the inhibitor drug to the patient continuously for the administration period when the current time measured by the time measurement unit coincides with the administration time by controlling the administration unit with the control unit.

14. An administration method to administer an inhibitor drug to a patient to inhibit cell division of a malignant cell, comprising the steps of:

20 setting an administration time to start an administration of the inhibitor drug to the patient on a basis of a predetermined phase of a cell cycle of the malignant cell, wherein a phase when a cell division inhibition effect by the inhibitor drug is

25

the highest is selected as the predetermined phase in the cell cycle, the cell cycle is divided into a plurality of groups by a predetermined period not more than a duration time of the predetermined phase, and the administration time is set plural times at not less than $(T + t)$ intervals if the cell cycle is made T , and the predetermined period is made t , and is set so that a difference of respective administration times for the plurality of groups is less than a two cycle period;

storing the set administration time in an administration time storage unit; and

administering the inhibitor drug to the patient continuously when the current time coincides with the administration time stored in the administration storage unit.

15. An administration apparatus substantially as hereinbefore described with reference to Figures 7A to 15D of the accompanying drawings.

16. An operating method of an administration apparatus substantially as hereinbefore described with reference to Figures 7A to 15D of the accompanying drawings.

17. An administration method substantially as hereinbefore described with reference to Figures 7A to 15D of the accompanying drawings.

FIG.1

NAME OF DRUG	DOSING STRATEGY
METHOTREXATE	<p>INFANT 1.25-2.5 MILLIGRAM CHILD 2.5-5 MILLIGRAM ADULT 5-10 MILLIGRAM PER DAY, INJECTED THREE TO SIX TIMES PER WEEK. INTRASTHECALLY INJECTED EVERY TWO TO SEVEN DAYS IN INJECTION DOSE OF 0.2-0.4 MILLIGRAM PER KILOGRAM OF BODY WEIGHT FOR PERIOSTEUM SYMPTOMS (PERIOSTEUM LEUKEMIA) BY MENINGEAL INFILTRATION OF LEUKEMIA.</p> <p>TROPHOBLASTIC DISEASE USUALLY INJECTED 10-30 MILLIGRAM PER DAY FOR ADULT AS METHOTREXATE MAKING FIVE DAYS A COURSE. DRUG HOLIDAYS USUALLY SEVEN TO TWELVE DAYS, BUT EXPANDED UNTIL SIDE EFFECT DISAPPEARS IF THE SIDE EFFECT OCCURS BY PREVIOUS INJECTION.</p>
EFFECTIVENESS	<p>SARCOMA: MORE THAN EFFECTIVENESS OF PULMONARY METASTASIS 20% ACUTE LEUKEMIA: EFFECTIVENESS 70% IF INEFFECTIVE TO OTHER DRUGS AND CENTRAL NERVOUS SYSTEM MOIST MALIGNANT LYMPHOMA: EFFICACY RATE 17% FOR SIX CASES OF MALIGNANT LYMPHOMA INEFFECTIVE TO OTHER DRUGS AND CENTRAL NERVOUS SYSTEM MOIST STOMACH CANCER: EFFICACY RATE 40.5% FOR 37 CASES</p>

FIG.2

NAME OF DRUG	DOSING STRATEGY
5-FLUOROURACIL	<p>A METHOD:</p> <ul style="list-style-type: none"> • LEVOFOLINATE 100 MILLIGRAM / SQUARE METER EVERY TIME (DRIP INJECTION FOR TWO HOURS) • INTRAVENOUS PUSH OF FLUOROURACIL 400 MILLIGRAM / SQUARE METER JUST AFTER FINISHED • MOREOVER, DRIP INJECTION FOR 22 HOURS OF FLUOROURACIL 400 MILLIGRAM / SQUARE METER <p>ABOVE ADMINISTRATION CONTINUOUSLY PERFORMED FOR TWO DAYS</p> <ul style="list-style-type: none"> • REPEATED EVERY TWO WEEKS
	<p>B METHOD:</p> <ul style="list-style-type: none"> • LEVOFOLINATE 250 MILLIGRAM / SQUARE METER EVERY TIME (DRIP INJECTION FOR TWO HOURS) • 24-HOUR CONTINUOUS INTRAVENOUS PUSH OF FLUOROURACIL 2600 MILLIGRAM / SQUARE METER JUST AFTER FINISHED <p>ABOVE ADMINISTRATION REPEATED SIX TIMES PER WEEK. DRUG HOLIDAYS FOR TWO WEEKS AFTER THAT</p> <p>ABOVE ADMINISTRATION MADE A COURSE</p>
	<p>C METHOD:</p> <ul style="list-style-type: none"> • LEVOFOLINATE 200 MILLIGRAM / SQUARE METER EVERY TIME (DRIP INJECTION FOR TWO HOURS) • INTRAVENOUS PUSH OF FLUOROURACIL 400 MILLIGRAM / SQUARE METER JUST AFTER FINISHED • MOREOVER, 46-HOUR DRIP INJECTION OF FLUOROURACIL 2400-3000 MILLIGRAM / SQUARE METER <ul style="list-style-type: none"> • REPEATED EVERY TWO WEEKS

FIG.3

TREATMENT	TEST TYPE	NUMBER OF CASES	RESPONSE RATE (%)	CR/PR(%)	SURVIVAL PERIOD MEDIAN SURVIVAL (MONTH)
Mayo	PHASE III	216	14	2/12	14.2
		167	12	0/12	11.9
De Gramont	PHASE III	217	32.6	6/27	15.5
AIO	PHASE III	164	17	2/15	13.7
Roswell Park (JAPAN)	PHASE II	70	30	0/30	9.9

FIG.4

NAME OF DRUG	DOSING STRATEGY
VINCRIStINE	<p>1. INJECTED INTRAVENOUSLY ONCE A WEEK 0.05-0.1 MILLIGRAM / KILOGRAM FOR CHILD, 0.02-0.05 MILLIGRAM / KILOGRAM FOR ADULT HOWEVER, SINGLE DOSE LESS THAN TWO MILLIGRAM TO AVOID SIDE EFFECT</p> <p>2. IF COMBINATION TREATMENT WITH OTHER ANTINEOPLASTIC DRUG AGAINST MULTIPLE MYELOMA IS PERFORMED, STANDARD DOSAGE AMOUNT AND ADMINISTRATION METHOD OF VINCRIStINE IS 24-HOUR CONTINUOUS INTRAVENOUS INJECTION OF 0.4 MILLIGRAM PER DAY IN COMBINATION USE WITH DOXORUBICIN HYDROCHLORIDE, DEXAMETHASONE SODIUM PHOSPHATE. AFTER THAT, HOLIDAY DRUG FOR 17-24 DAYS IS TAKEN. ABOVE IS MADE A COURSE, AND ADMINISTRATION IS REPEATED.</p> <p>3. IF COMBINATION TREATMENT WITH OTHER ANTINEOPLASTIC DRUG AGAINST GLIOMA INCLUDING MALIGNANT ASTROCYTOMA MULTIPLE AND OLIGODENDROGLIOMA COMPONENT MYELOMA IS PERFORMED, INTRAVENOUS INJECTION OF 1.4 MILLIGRAM / SQUARE METER IS PERFORMED TWO TIMES AS VINCRIStINE SULFATE. SECOND ADMINISTRATION IS PERFORMED AFTER THREE WEEKS OF FIRST ADMINISTRATION, AND ADMINISTRATIONS ARE REPEATED, MAKING SIX TO EIGHT WEEKS A COURSE. HOWEVER, SINGLE DOSE IS LESS THAN TWO MILLIGRAM TO AVOID SIDE EFFECT.</p>

FIG.5

DISEASE NAME	NUMBER OF CLINICAL CASES	NUMBER OF REMISSION CASES	REMISSION RATE (%)
LEUKEMIA: ACUTE LEUKEMIA (CHILD)	42	26	61.9
LEUKEMIA: ACUTE LEUKEMIA (ADULT)	4/	1/	36.2
LEUKEMIA: ACUTE LEUKEMIA (SUBTOTAL)	89	43	48.3
LEUKEMIA: CHRONIC LEUKEMIA (BLAST CRISIS)	3	2	66.7
MALIGNANT LYMPHOMA: RETICULOSARCOMA	21	15	71.4
MALIGNANT LYMPHOMA: LYMPHOSARCOMA	16	10	62.5
MALIGNANT LYMPHOMA: HODGKIN' S DISEASE	19	16	84.2
MALIGNANT LYMPHOMA: SUBTOTAL	56	41	73.2
CHILDHOOD TUMOR: NEUROBLASTOMA	12	8	66.7
CHILDHOOD TUMOR: WILMS' TUMOR	2	2	
CHILDHOOD TUMOR: EMBRYONAL TESTICULAR CANCER	2	2	
CHILDHOOD TUMOR: RHABDOMYOSARCOMA	2	1	
CHILDHOOD TUMOR: ANGIOSARCOMA	1	1	
CHILDHOOD TUMOR: OSTEOSARCOMA	1	0	
CHILDHOOD TUMOR: RETINOBLASTOMA	1	0	
CHILDHOOD TUMOR: LIPOSARCOMA	1	0	
CHILDHOOD TUMOR: ADRENAL CORTEX CANCER	1	0	
CHILDHOOD TUMOR: SUBTOTAL	23	14	60.9

FIG.6

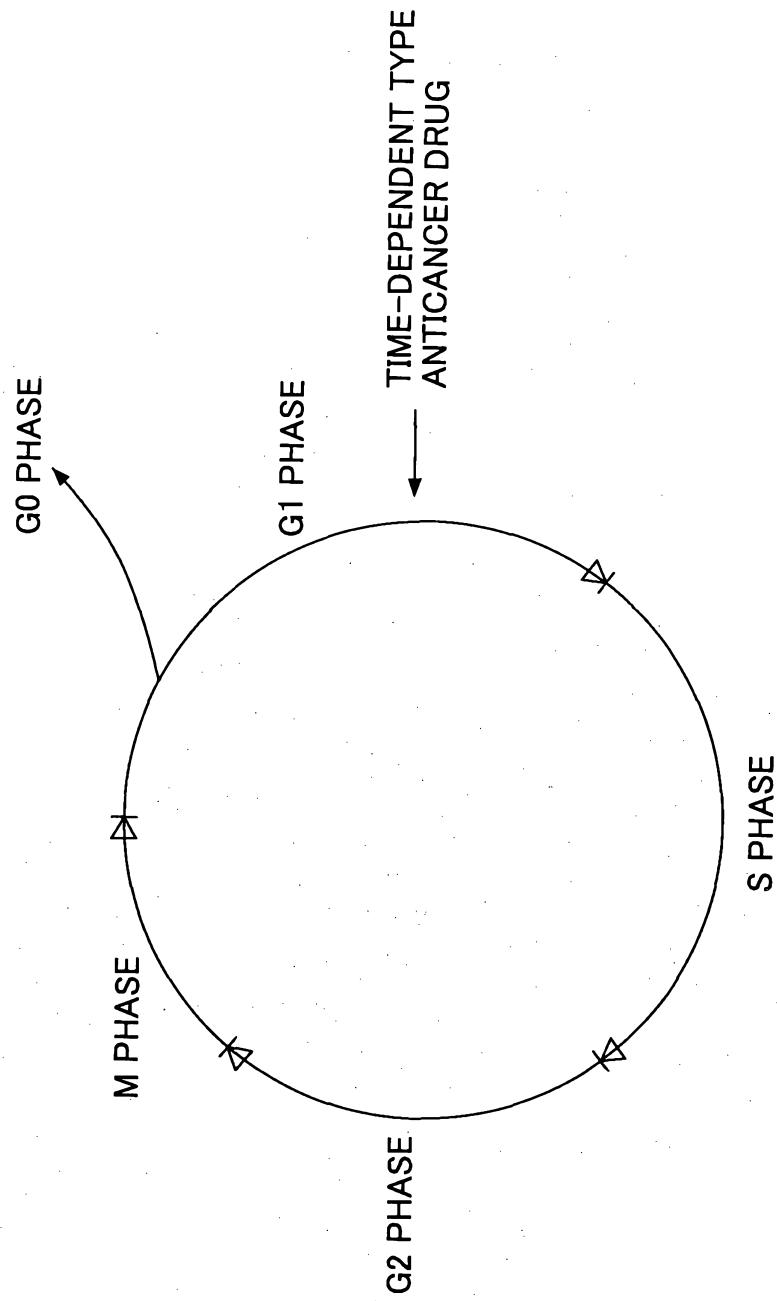
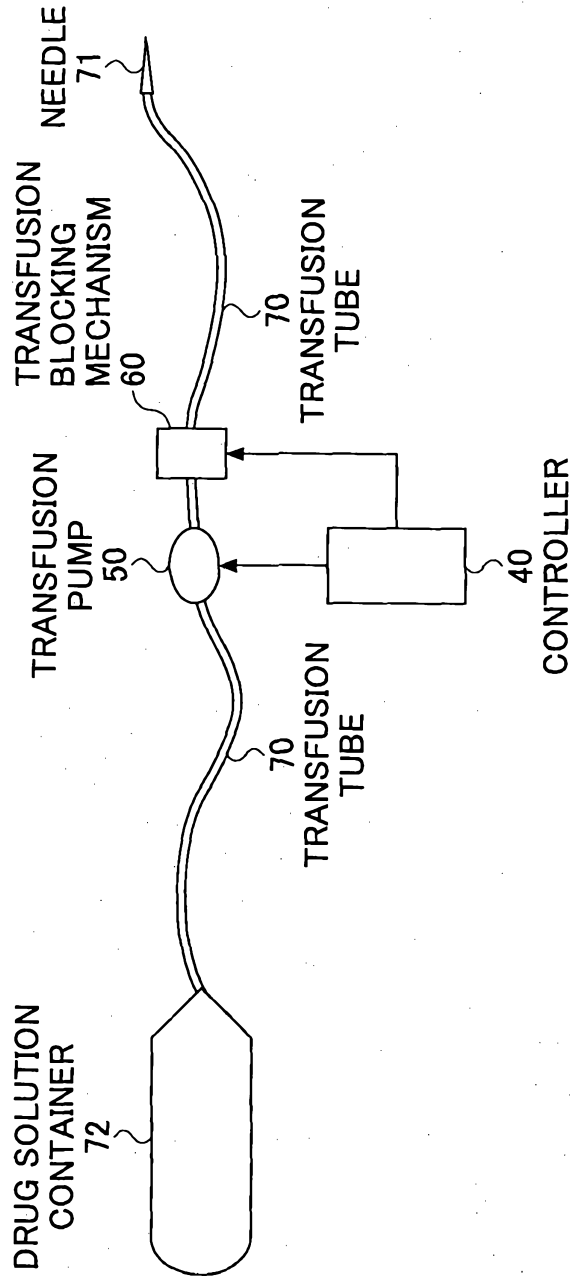


FIG.8



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FIG.9

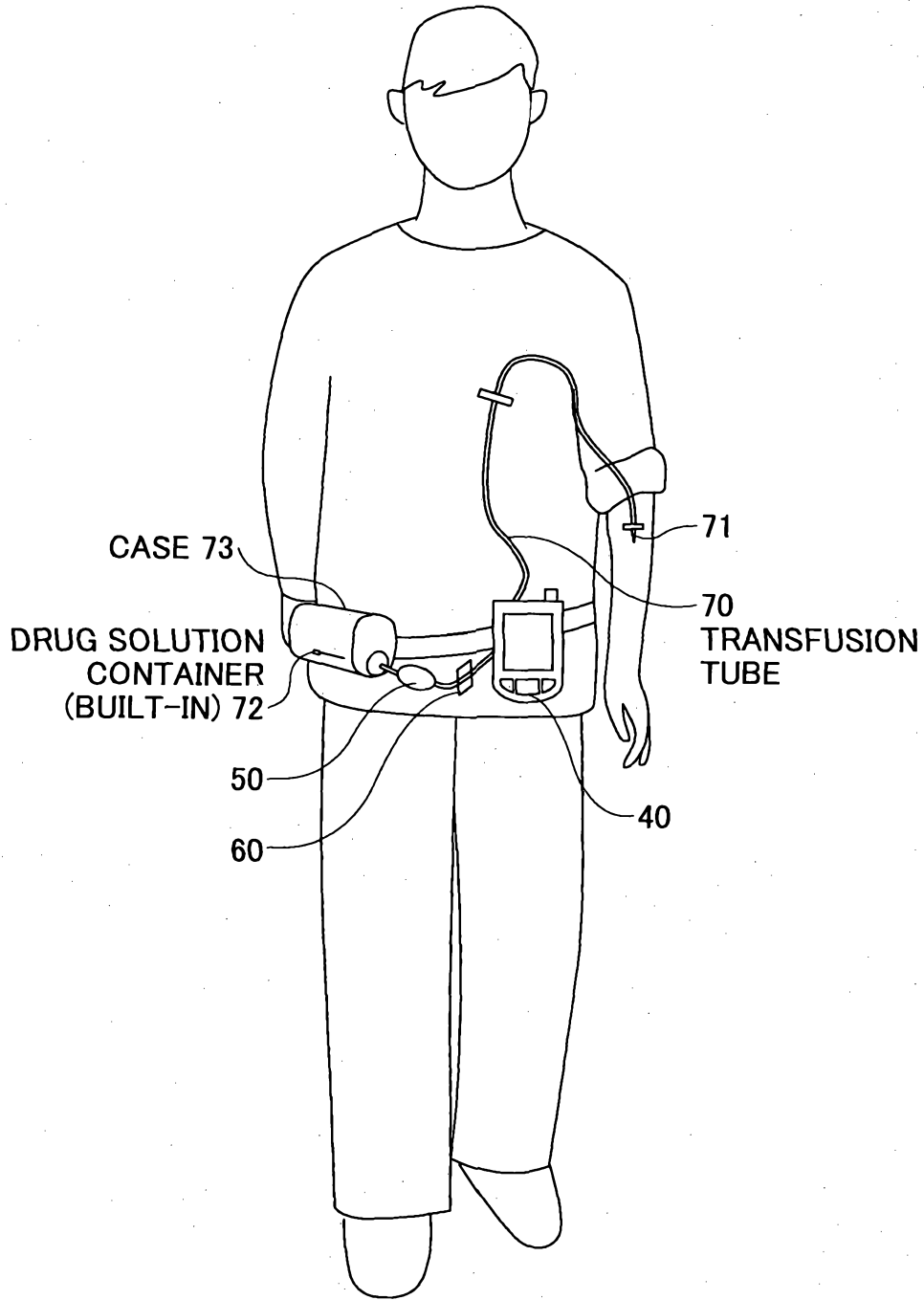
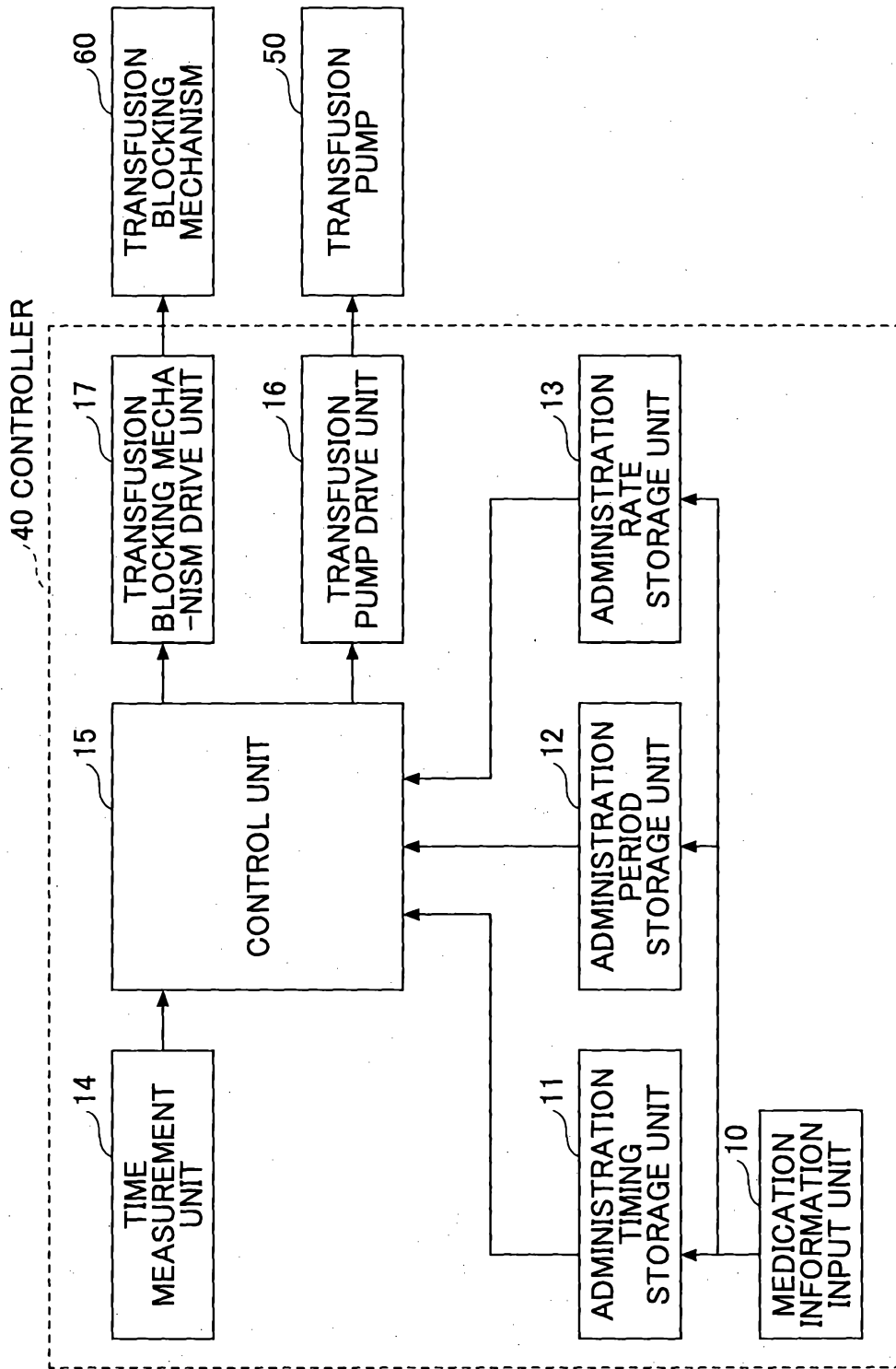
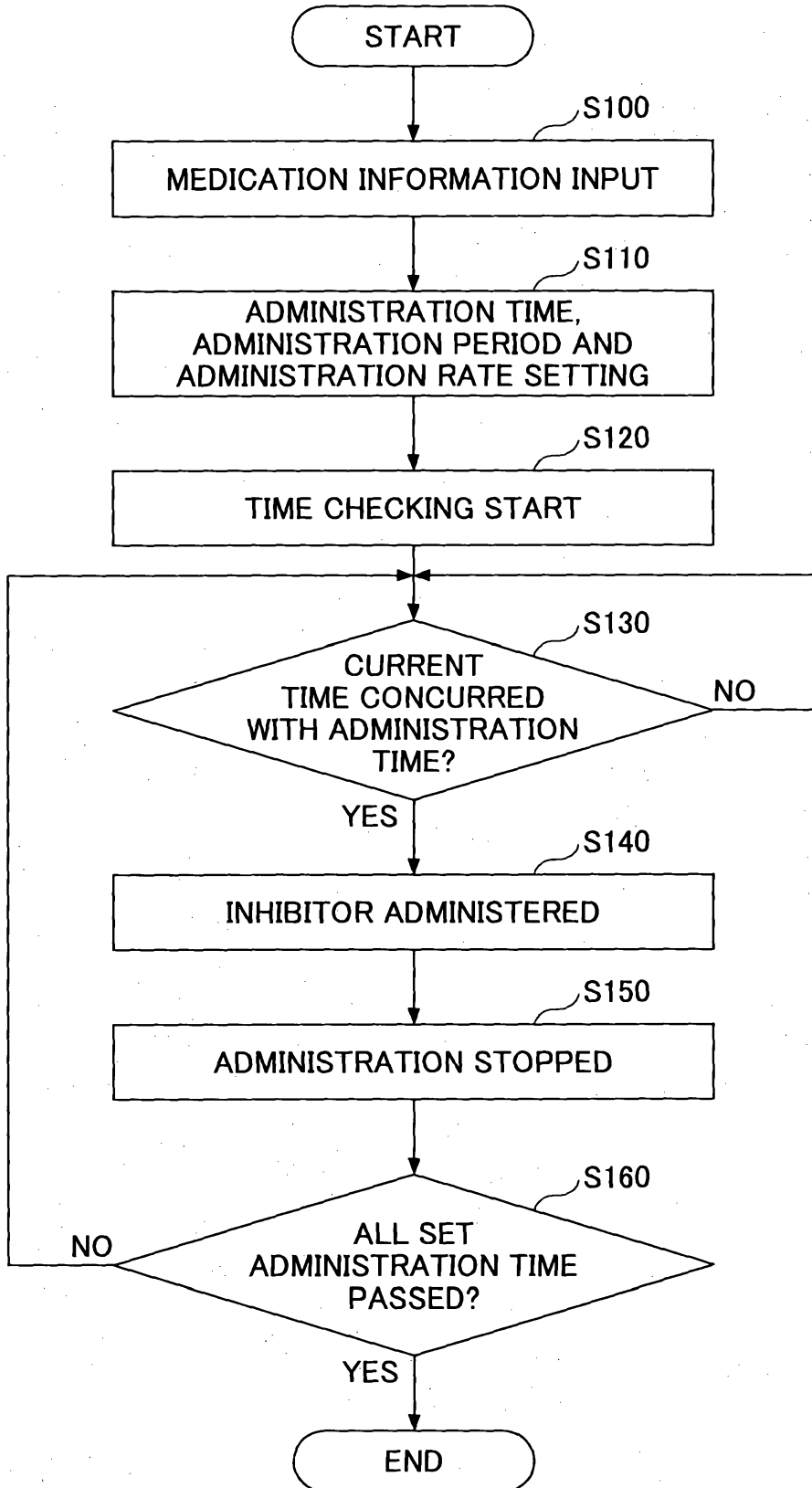


FIG.10



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FIG.11



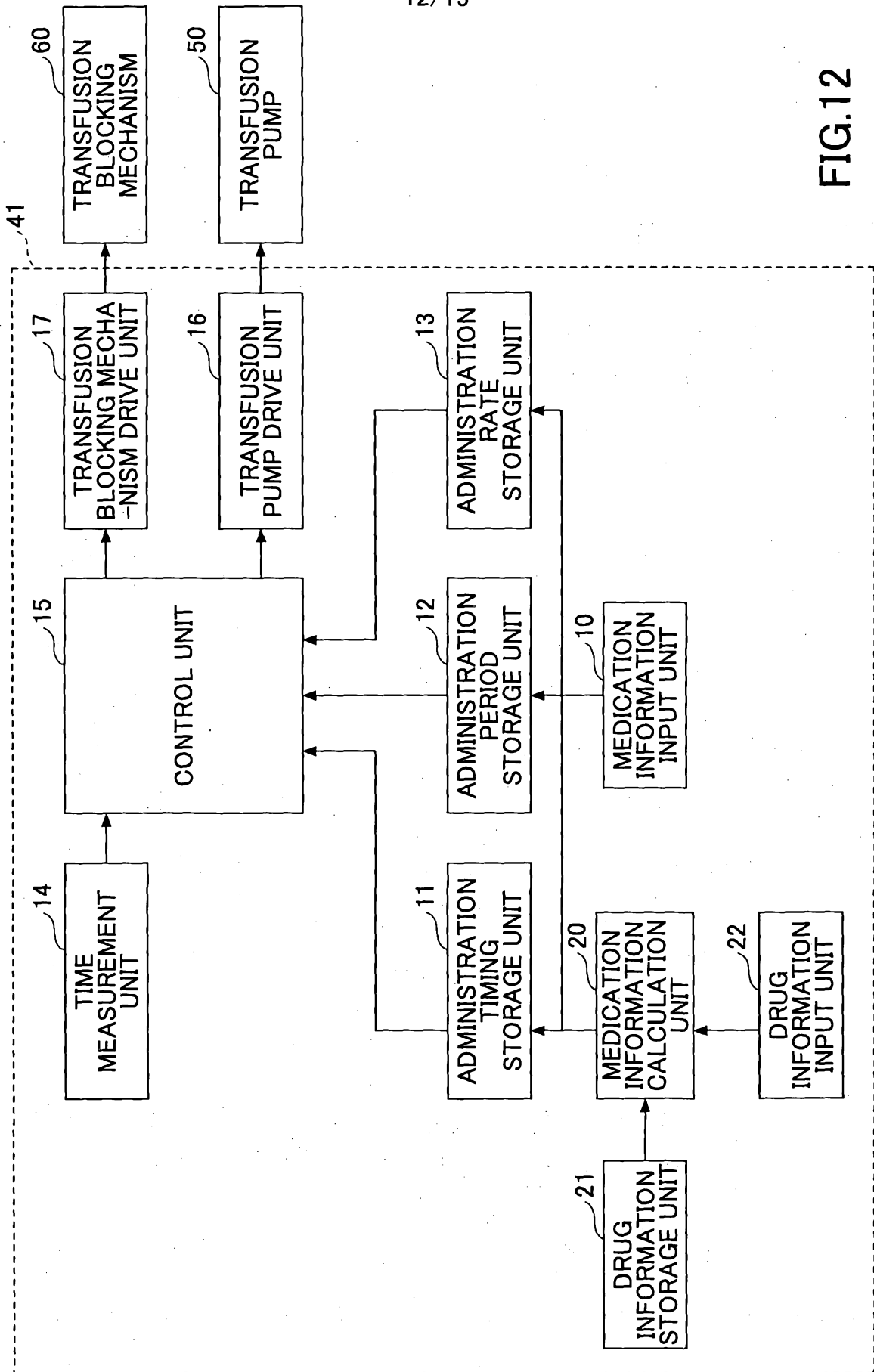


FIG.12

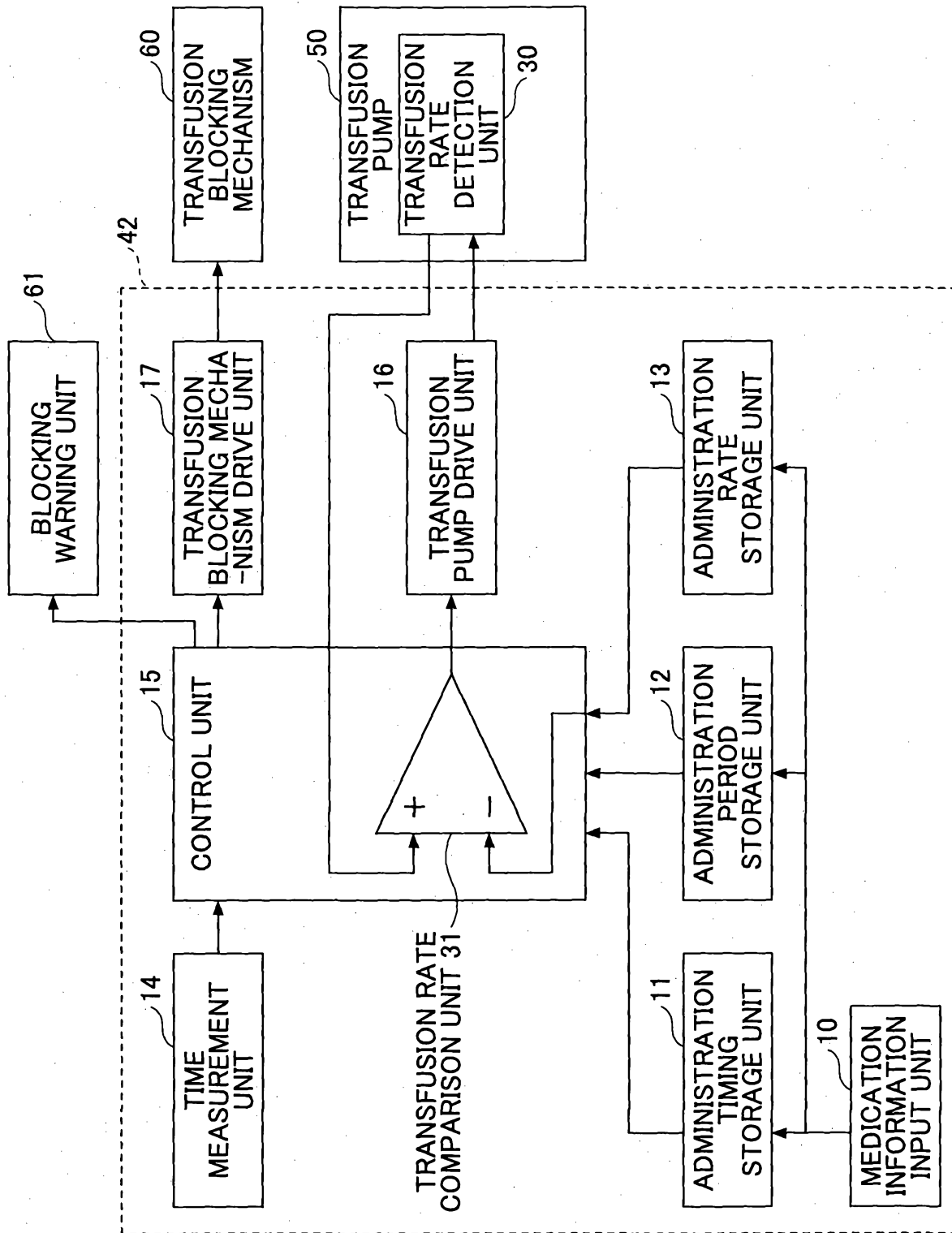


FIG.13

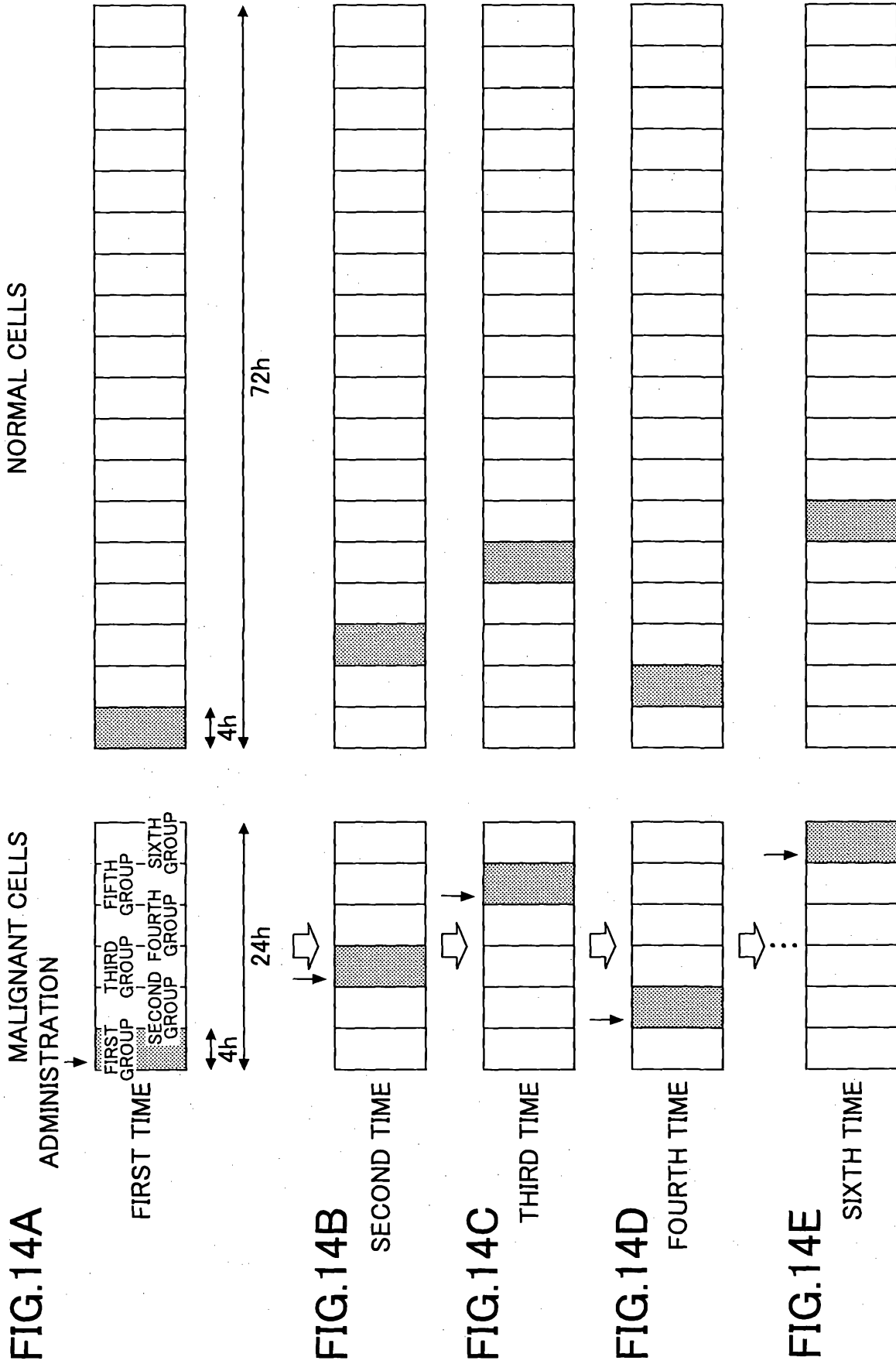


FIG.15A

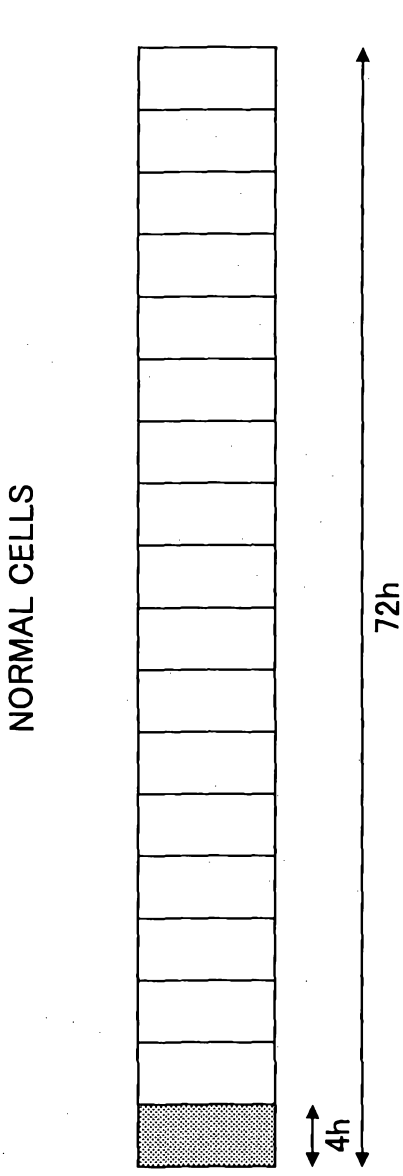


FIG.15B

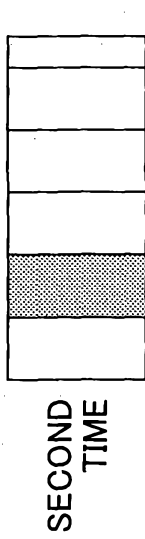


FIG.15C

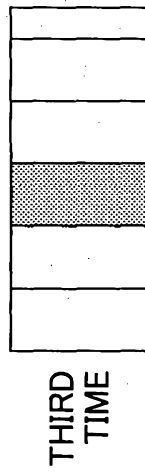


FIG.15D

