Pressure Compatibility Test of Closed System Drug Transfer Devices for 71 Anticancer Drugs

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Occupational exposure to anticancer drugs may increase the risk of cancer and the risk of miscarriage and stillbirth, and cause other adverse events such as hypersensitivity reactions, skin/mucous reactions, and digestive symptoms. Several studies have investigated the use of closed-system drug-transfer devices (CSTDs) to reduce the environmental pollution by hazardous drugs. However, few reports have verified whether CSTDs contain the hazardous drugs within the vials. The BD PhaSeal™ System is a CSTD that is frequently used in Japan. However, the fit of each anti-cancer drug vial has not been investigated. We investigated the fit of 71 major anti-cancer drug vials and protectors released and frequently used in Japan by means of a pressure compatibility test that we developed. The pressure compatibility test involved attaching a three-way stopcock to a Luer lock syringe and attaching an injector in line with the syringe. The pressure tubing was connected to the other side of the three-way stopcock and connected to the pressure inlet of the pressure gauge. The pressure in the anti-cancer drug vial was raised to 100 kPa and connected/disconnected repeatedly. If the pressure fluctuation during the 10th connection was within 6%, it was defined as “no change”, and the compatibility of the protector and the vial was evaluated. The median pressure reduction rates at the 10th connection ranged from −1.98% to −4.95%. All drugs surveyed had an error rate within 6%. The BD PhaSeal™ Protector was shown to be compatible with the 71 anti-cancer drugs we surveyed.

Key words—hazardous drug vial; closed system drug transfer devise; compatibility pressure

INTRODUCTION

The risk of occupational exposure to anti-cancer drugs was reported by Falck et al. in 1979 and is highlighted as the first toxicity report for health care workers.1) The National Institute of Occupational Safety and Health (NIOSH) defined hazardous drugs as anti-cancer drugs and similarly toxic substances that have carcinogenicity, teratogenicity, developmental toxicity, reproductive organ toxicity, low-dose organ toxicity, and genotoxicity in humans and animals.2) Exposure of health workers to hazardous drugs has remained a problem ever since the health risks were reported.2,3) To reduce exposure, NIOSH issued the NIOSH Alert in 2004 to warn employees and employers dealing with hazardous drugs.2) USP (800), which came into effect in December 2019, strongly recommends the use of a safety cabinet or an isolator installed in a negative pressure preparation room of ISO class 5 and closed-system drug-transfer devices (CSTDs) when preparing hazardous drugs.4)

Although it depends on the drug, medical personnel exposed to hazardous drugs may be at increased risk of cancer,5–8) miscarriage and stillbirth,9,10) and other adverse effects such as hypersensitivity reactions, skin/mucous membrane reactions, digestive symptoms, cardiovascular symptoms, respiratory symptoms, and neurological symptoms.11,12) A CSTD is defined in NIOSH Alert 2004 and ISOPP Standards and Practice 2007 as a device “mechanically suppressing the transfer of environmental pollution to another system and keeping hazardous drugs and volatile pollution out of the system”.2,13) Several reports have investigated the use of CSTDs for reducing environmental pollution by hazardous drugs.14–19) In these studies, preparation place and environmental pollution around it were investigated to determine the effectiveness of exposure countermeasures when using CSTDs to prepare hazardous drugs. Environmental contamination was evaluated by wiping safety cabinets or the surfaces of preparation tables, not by checking whether hazardous drugs leaked from vials. Few studies have directly verified whether CSTDs contain hazardous drugs within the vials.

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The BD PhaSeal™ System (Becton, Dickinson and Company, Franklin Lakes), which is a CSTD frequently used in Japan, is a device that allows a BD PhaSeal™ Protector (hereinafter, “protector”) of an appropriate size to be fitted onto a rubber stopper of the vial, and enables the drug solution in the vial to be collected by a syringe equipped with BD PhaSeal™ Injector N35 (hereinafter, “injector”) without scattering the solution. The protector features an expansion bladder that has a pressure-equalizing function that pressurizes the vial. However, a previous study found that the expansion bladder could be safely pressurized to 100 kPa after it had fully expanded. By pressurizing the inside of the vial, even a very small leak that could not otherwise be measured by the built-in pressure gauge can be detected as a pressure leak by the pressure gauge. This allows the “nothing in, nothing out” requirement that is critical to the function of CSTDs to be tested. If the pressure drop is below the specified value even when the inside of the vial is pressurized and the injector has been connected multiple times, then it is assured that no leaks from the CSTDs will occur. In Japan, the BD PhaSeal™ System is available in six variations, each with different vial port diameters and expansion bladder capacities. However, in countries such as Japan where there are no regulations regarding the shape standards of vials for pharmaceutical products, vials are available in various sizes with different diameters and heights. Therefore, when the protector is fitted, it may not be fixed to the vial, which may cause a problem with the tightness between the protector and the vial. Moreover, if the rubber stopper of the vial is dented, a gap may open between the rubber stopper and the sealing rim of the protector, and the hermeticity may be impaired. If the hermeticity is impaired, gas containing the hazardous drug may leak out from the gap when it is extracted from the vial, and also the hazardous drugs may be contaminated. The precautionary statement in the package insert states that users must ensure “the protector is fully attached to the vial”. Therefore, it is essential to select an appropriate protector that is compatible with the vial.

Some studies have investigated the compatibility between protectors and anti-cancer drug vials; one investigated whether the diameters and heights of the rubber stopper met the specifications of the protectors and another released a leak test report of titanium tetrachloride smoke. In the first study, which investigated whether the diameter and height of the rubber stopper met the specifications of the protector, the diameters and heights of the vial ports were visually inspected and both the safety and operability when connecting the protector was confirmed. However, the hermeticity was not objectively evaluated. The investigation using titanium tetrachloride smoke enabled visualization of air leaks as smoke from a CSTD, but it is difficult to detect the smoke when the leak is small. There are few studies that have objectively verified the hermeticity between the protector and hazardous drugs vials. We previously developed a method to monitor the tightness between BD PhaSeal™ System and hazardous drug vials at medical institutions by monitoring the fluctuation of the internal pressure of the vial with a simple pressure gauge. The test method involved fitting a protector into vials containing sterile water for injection and increasing the vial pressure to 100 kPa. Then, the injector and protector were connected/disconnected 10 times, and the internal pressure of the vial at each connection was measured. This study showed that the pressure in the vial at the time of the first connection was reduced by 85% by the 10th connection in vials that cannot maintain the seal between the sealing rim on the back of the protector and the rubber stopper of the vial.

In the present study, we used this method to investigate the hermeticity of protectors and vials for domestically marketed anti-cancer drug vials in Japan, and constructed a database of compatibility between anti-cancer drug vials and protectors.

**MATERIALS AND METHODS**

We tested 71 types of anti-cancer drug vials frequently used in Japan. Five vials were tested for each drug.

A protector (P53J, P50J, or P14J) was fitted to the anti-cancer drug vial using the BD PhaSeal™ assembly fixture. A 50 mL Luer lock syringe (SS-50LZ, Terumo Corp., Tokyo) was fitted with a TELFUSION® three-way stopcock (TS-TR2A, Terumo Corp.), and an injector was attached so that it was in line with the syringe. On the other side of the three-way stopcock, the pressure tubing (PT06M, 15 cm, Lot: 405745, Argon Medical Devices, Frisco) was connected to pressure tubing with an outer diameter of 6 mm and connected to the pressure inlet of the pressure gauge (GC66, Nagao Keiki Co., Ltd.,
The pressure test equipment has already been reported.\textsuperscript{23} The specifications of the pressure gauge are as follows: differential pressure range, 0 to 500 kPa; accuracy, ± (1.0\% F.S. + 1 digit); and display cycle, 2 times/s.

The test drug vial that the protector was fitted to was set in the pressure experiment device, and the pressure in the vial was manually increased to 100 kPa. The vial fitted with the protector and the injector were connected and disconnected 10 times at 5-s intervals, and the internal pressure of the vial was measured at each connection. This was performed 5 times for each test drug, and the medians were calculated. The results were defined as “no change” when the pressure fluctuation during the 10th connection of the anticancer drug vial was within $6\%$ because there is a $6\%$ error in the pressure gauge.

\section*{RESULTS}

Table 1 shows the pressure reduction rate at the 10th connection of the 71 anticancer drugs in the pressure compatibility test. Tests were performed 5 times for each drug, except for a few instances in which tests were performed only 4 times due to damage to the protector. The median values of the pressure reduction rates at the 10th connection ranged from $-1.98\%$ to $-4.95\%$. The drugs with the largest pressure decrease ($-4.95\%$) were Docetaxel I.V. Infusion 20 mg/2 mL, 80 mg/4 mL, and 120 mg/12 mL Hospira; Docetaxel I.V. Infusion 80 mg/4 mL “Yakult”; Paclitaxel Inj. 100 mg/16.7 mL and 30 mg/5 mL “NK”; and Navelbine Injection 10 and 40. The drug with the smallest pressure decrease ($-1.98\%$) was Fildesin 1 mg. It was shown that all test drugs investigated in this study had an error rate within $6\%$ and were compatible with the protector.

\section*{DISCUSSION}

This study aimed to investigate the compatibility between vials of anti-cancer drugs, which are considered hazardous drugs, and the protector. We also created a database of anti-cancer drugs that can be prepared safely using CSTDs. The compatibility levels of all 71 hazardous drugs investigated in this study with the protector were good.

The drugs tested were selected because they are those used in the main chemotherapy regimens in Japan and constitute some of the drugs listed in NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016.\textsuperscript{24} According to a questionnaire survey conducted by the Japan Hospital Pharmacists Association, the usage rate of CSTDs for three drugs, namely, cyclophosphamide, ifosfamide, and bendamustine, was about $70\%$ in facilities with 500 or more beds in Japan, while the usage rate of CSTDs for other anti-cancer drugs was only $6.4\%$.\textsuperscript{25} However, the NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings comprises 115 anti-cancer drugs and 102 drugs other than anti-cancer drugs, including those not yet approved in Japan.\textsuperscript{20} Therefore, at least when preparing the drugs listed in the NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, measures against occupational exposure should be taken considering the safety of medical staff. The advantage of using CSTDs is that the preparation can be performed with a high level of control, regardless of staff experience in the preparation of anticancer drugs, compared with conventional methods. There are also some reports showing that preparation time can be shortened by using a CSTD rather than the conventional method of using an injection needle.\textsuperscript{26,27}

Regarding the formation of pinholes by repeated punctures, Hama \textit{et al.} reported that no fluorescent dye leaked following up to 30 punctures using a “protector sorus”\textsuperscript{28}. Among the anti-cancer drug vials we tested, the largest pressure decrease was $-4.95\%$ for Paclitaxel Injection 100 mg/16.7 mL “NK”, Paclitaxel Injection 30 mg/5 mL “NK”, and Navelbine Injections 10 and 40, while the smallest pressure decrease was $-1.98\%$ for Fildesin 1 mg. We determined that all tested anti-cancer drug vials conformed with the standards. We considered that the $-4.95\%$ to $-1.98\%$ pressure reductions were not due to pressure leaking out of the pressure test equipment, but instead due to the inside of the vial, the inside of the injection needle of the injector, the three-way stop-cock, the pressure gauge, and the inside of the syringe being pressurized at the time of connection, while the interior space of the injector was not. We believe that the slight decrease in pressure of $-4.95\%$ to $-1.98\%$ was due to the following: when the injector was disconnected, the inside of the injector was pressurized when the injection needle was returned to the inside of the injector, which was not pressurized. Therefore, the pressure in the vial decreased until the third connection, as the inside of the injector was filled, and
## Table 1. Compatibility Test Results between Protector and Test Drug \( (n = 5) \)

| Generic name                  | Drug name                      | Lot.   | Protector | Median (Range) | Compatibility | Company                        |
|-------------------------------|--------------------------------|--------|-----------|----------------|---------------|---------------------------------|
| Amrubicin hydrochloride       | Calsed 20 mg                   | 470010 | P50J      | -1.98          | -0.99 to -2.97 | ○                               | Sumitomo Dainippon Pharma Co., Ltd. (Osaka) |
|                               |                                |        |           |                |               |                                 |                                              |
| Carboplatin                   | Carboplatin 450 mg “NICHIIKO”  | B00300 | P50J      | -2.97          | -0.99 to -2.97 | ○                               | Nichi-Iko Pharmaceutical Co., Ltd. (Tokyo)   |
|                               | Carboplatin 150 mg “NICHIIKO”  | B00100 | P50J      | -2.97          | -0.99 to -2.97 | ○                               |                                              |
|                               | Carboplatin 50 mg “NICHIIKO”   | BV0100 | P50J      | -2.97          | -0.99 to -2.97 | ○                               |                                              |
| Carboplatin                   | Carboplatin 450 mg “NK”        | X61910 | P50J      | -2.97          | -0.99 to -3.00 | ○                               | Nippon Kayaku Co., Ltd. (Tokyo)             |
|                               | Carboplatin 150 mg “NK”        | 861650 | P50J      | -3.00          | -0.99 to -3.00 | ○                               |                                              |
|                               | Carboplatin 50 mg “NK”         | 760710 | P50J      | -3.00          | -0.99 to -4.00 | ○                               |                                              |
|                               | CARBOPLATIN 450 mg “SAWAI”     | 15902  | P50J      | -1.98          | -0.99 to -2.97 | ○                               | Sawai Pharmaceutical Co., Ltd. (Osaka)      |
|                               | CARBOPLATIN 150 mg “SAWAI”     | 15Y01  | P50J      | -2.97          | -0.99 to -3.96 | ○                               |                                              |
|                               | CARBOPLATIN 50 mg “SAWAI”      | 15601  | P50J      | -2.97          | -0.99 to -4.00 | ○                               |                                              |
|                               | PARAPLATIN INJECTION 50 mg     | AAU8186 | P50J    | -2.97          | -0.99 to -3.00 | ○                               | Bristol-Myers Squibb Company (Tokyo)         |
|                               |                                |        |           |                |               |                                 |                                              |
| Cisplatin                     | Cisplatin 10 mg “NICHIIKO”     | B00400 | P50J      | -2.97          | -0.99 to -2.97 | ○                               | Nichi-Iko Pharmaceutical Co., Ltd. (Tokyo)   |
|                               | Cisplatin 25 mg “NICHIIKO”     | LR2500 | P50J      | -2.00          | -0.99 to -2.97 | ○                               |                                              |
|                               | Cisplatin 50 mg “NICHIIKO”     | B00880 | P53J      | -2.97          | -0.99 to -2.97 | ○                               |                                              |
|                               |                                |        |           |                |               |                                 |                                              |
| Cyclophosphamide hydrate      | Endoxan 100 mg                 | 4417   | P50J      | -2.97          | -0.99 to -2.97 | ○                               | Shionogi & Co., Ltd. (Osaka)                |
|                               | Endoxan 500 mg                 | 4426   | P50J      | -2.00          | -0.99 to -2.97 | ○                               |                                              |
|                               |                                |        |           |                |               |                                 |                                              |
| Docetaxel                     | Docetaxel I.V. Infusion 120 mg/12 mL Hospira | C022264AA | P50J | -4.95 | -0.99 to -4.95 | ○ | Pfizer Japan Inc. (Tokyo) |
|                               | Docetaxel I.V. Infusion 80 mg/8 mL Hospira | C042263AA | P50J | -4.95 | -0.99 to -4.95 | ○ |                                              |
|                               | Docetaxel I.V. Infusion 20 mg/2 mL Hospira | C032262AA | P50J | -4.95 | -0.99 to -4.95 | ○ |                                              |
|                               |                                |        |           |                |               |                                 |                                              |
|                               | Docetaxel I.V. Infusion 80 mg/4 mL “Yakult” | DLABAA | P50J | -4.95 | -0.99 to -4.95 | ○ | Yakult Honsha Co., Ltd. (Tokyo) |
|                               | Docetaxel I.V. Infusion 20 mg/1 mL “Yakult” | DKAakra | P50J | -4.95 | -0.99 to -4.95 | ○ |                                              |
|                               |                                |        |           |                |               |                                 |                                              |
|                               | ONE TAXOTERE 20 mg/1 mL         | 8D024A | P50J      | -2.97          | -0.99 to -3.96 | ○                               | Sanofi K.K. (Tokyo)                          |
|                               |                                |        |           |                |               |                                 |                                              |
| Doxorubicin hydrochloride     | ADRIACIN Injection 10 mg        | 521AFE | P50J      | -2.97          | -0.99 to -3.96 | ○                               | Kyowa Kirin Co., Ltd. (Tokyo)               |
|                               | ADRIACIN Injection 50 mg        | 037AFF | P50J      | -2.97          | -0.99 to -3.96 | ○                               |                                              |
|                               |                                |        |           |                |               |                                 |                                              |
| Fluorouracil                  | 5-FU Injection 1000 mg          | 18303LF | P50J    | -1.98          | -0.99 to -1.98 | ○                               | Kyowa Kirin Co., Ltd. (Tokyo)               |
|                               |                                |        |           |                |               |                                 |                                              |
|                               | FLUOROURACIL INJECTION 1000 mg “TOWA” | D043 | P50J | -2.97 | -0.99 to -3.96 | ○ | Towa Pharmaceutical Co., Ltd. (Osaka) |
|                               | FLUOROURACIL INJECTION 250 mg “TOWA” | D013A | P50J | -2.97 | -0.99 to -3.96 | ○ |                                              |
| Generic name | Drug name | Lot. | Protector | Median (Range) | Compatibility | Company |
|--------------|-----------|------|-----------|----------------|---------------|---------|
| Gemcitabine for I.V. Infusion 1 g "NK" | 960360 P50J | -2.97 | -2.00 to -2.97 | ◯ | Nippon Kayaku Co., Ltd. (Tokyo) |
| Gemcitabine for I.V. Infusion 200 mg "NK" | 860170 P50J | -2.97 | -2.97 to -2.97 | ◯ | |
| Gemcitabine hydrochloride | AG2700 P50J | -2.97 | -2.97 to -4.95 | ◯ | Nichi-Iko Pharmaceutical Co., Ltd. (Tokyo) |
| Gemcitabine 1 g "NICHIIKO" | 27000 P50J | -2.97 | -2.97 to 4.95 | ◯ | Nichi-Iko Pharmaceutical Co., Ltd. (Tokyo) |
| Gemcitabine 200 mg "NICHIIKO" | 85000 P50J | -2.97 | -2.00 to -3.95 | ◯ | |
| Gemzar Injection 1 g | C574798AA P50J | -2.97 | -2.97 to -3.00 | ◯ | Eli Lilly Japan K.K. (Kobe) |
| Gemzar Injection 200 mg | C573111AA P50J | -1.98 | -0.99 to -2.97 | ◯ | |
| Ifosfamide | Ifomide | 4143 P50J | -1.98 | -0.99 to -2.97 | ◯ | Shionogi & Co., Ltd. (Osaka) |
| Irinotecan hydrochloride hydrate | Irinotecan Hydrochloride 40 mg | LR0705 P50J | -2.97 | -2.97 to -4.95 | ◯ | Nichi-Iko Pharmaceutical Co., Ltd. (Tokyo) |
| Irinotecan Hydrochloride 100 mg | LR0502 P50J | -2.97 | -2.00 to -3.00 | ◯ | |
| Methotrexate | METHOTREXATE INJECTION 200 mg | 16M01A P50J | -2.97 | -2.97 to -4.95 | ◯ | Pfizer Japan Inc. (Tokyo) |
| Mitomycin C | MITOMYCIN Injection 10 mg | 130AFE P50J | -2.97 | -2.97 to -3.96 | ◯ | Kyowa Kirin Co., Ltd. (Osaka) |
| Mitomycin C | MITOMYCIN Injection 2 mg | 580AFD P50J | -2.97 | -2.97 to -4.00 | ◯ | |
| Oxaliplatin | ELPLAT I. V. INFUSION SOLUTION 200 mg | XHBJGA P50J | -2.97 | -2.97 to -2.97 | ◯ | Yakult Honsha Co., Ltd. (Tokyo) |
| Oxaliplatin | ELPLAT I. V. INFUSION SOLUTION 100 mg | XJABE A P50J | -2.97 | -2.97 to -4.95 | ◯ | |
| Oxaliplatin | ELPLAT I. V. INFUSION SOLUTION 50 mg | XGADBA P50J | -2.97 | -2.00 to -2.97 | ◯ | |
| Oxaliplatin | OXALIPLATIN INTRAVENOUS INFUSION 200 mg "TOWA" | D002 P50J | -2.00 | -2.00 to -2.97 | ◯ | Towa Pharmaceutical Co., Ltd. (Osaka) |
| Oxaliplatin | OXALIPLATIN INTRAVENOUS INFUSION 100 mg "TOWA" | D008 P50J | -4.46 | -2.97 to -4.95 | ◯ | |
| Oxaliplatin | OXALIPLATIN INTRAVENOUS INFUSION 50 mg "TOWA" | D002A P50J | -2.97 | -2.97 to -4.95 | ◯ | |
| Oxaliplatin | OXALIPLATIN 200 mg/40 mL “SAWAI” | 15401 P50J | -2.97 | -0.99 to -2.97 | ◯ | Sawai Pharmaceutical Co., Ltd. (Osaka) |
| Oxaliplatin | OXALIPLATIN 100 mg/20 mL “SAWAI” | 15301 P50J | -2.97 | -2.00 to -2.97 | ◯ | |
| Oxaliplatin | OXALIPLATIN 50 mg/10 mL “SAWAI” | 15502 P50J | -2.97 | -2.97 to -4.00 | ◯ | |
| Oxaliplatin | Oxaliplatin I.V. Infusion 200 mg/40 mL Hospira | C015357AA P50J | -2.97 | -2.00 to -2.97 | ◯ | Pfizer Japan Inc. (Tokyo) |
| Oxaliplatin | Oxaliplatin I.V. Infusion 100 mg/20 mL Hospira | B025354AB P50J | -2.97 | -2.97 to -3.96 | ◯ | |
| Oxaliplatin | Oxaliplatin I.V. Infusion 50 mg/10 mL Hospira | D015353AA P50J | -2.97 | -2.97 to -4.00 | ◯ | |
the pressure in the vial after the fourth connection did not change. We found that there were no problems in compatibility between the anticancer drug vials and the protector investigated in this study, suggesting that leakage of anticancer drugs can be prevented by performing correct operations when preparing the tested drugs using a protector. We confirmed that we could meet the “Nothing Out” condition of CSTDs, as defined by NIOSH and ISOPP standards.

In investigations of environmental pollution during the preparation of hazardous drugs, the effects of exposure control have been discussed in measurements of the concentration of hazardous drugs in the work environment and the surrounding area by the wipe and sampling sheet methods.14–16,19,28 When determining the compatibility between hazardous drugs and protectors, the diameter and height of the rubber stopper is measured, and whether it is within the specifications of the protector is evaluated.21 Few studies have examined the leakage of hazardous drugs during preparation. In our study, the pressure fluctuation in the vial was monitored over time when the CSTD was repeatedly connected and disconnected 10 times (corresponding to draining the drug solution in the vial 10 times), and the compatibility between the anticancer drug vial and protector was monitored.

| Generic name | Drug name | Lot. | Protector | Median (Range) | Compatibility | Company |
|--------------|-----------|-----|-----------|----------------|---------------|---------|
| Oxaliplatin  | Oxaliplatin I.V. Infusion Solution 200 mg “NK” | 760060 | P50J | $-2.97$ (-0.99 to -2.97) | ◯ | Nippon Kayaku Co., Ltd. (Tokyo) |
|              | Oxaliplatin I.V. Infusion Solution 100 mg “NK” | X60200 | P50J | $-2.97$ (-2.97 to -3.96) | ◯ | Nippon Kayaku Co., Ltd. (Tokyo) |
|              | *Oxaliplatin I.V. Infusion Solution 50 mg “NK” | 860070 | P50J | $-2.97$ (-2.97 to -2.97) | ◯ | Nippon Kayaku Co., Ltd. (Tokyo) |
|              | OXALIPLATIN 200 mg “NICHIIKO” | BG1600 | P50J | $-1.98$ (-1.98 to -2.97) | ◯ | Nichi-Iko Pharmaceutical Co., Ltd. (Tokyo) |
|              | OXALIPLATIN 100 mg “NICHIIKO” | BG1700 | P50J | $-4.00$ (-1.98 to -4.00) | ◯ | Nippon Kayaku Co., Ltd. (Tokyo) |
|              | OXALIPLATIN 50 mg “NICHIIKO” | BG1200 | P50J | $-2.97$ (-2.97 to -4.95) | ◯ | Nippon Kayaku Co., Ltd. (Tokyo) |
| Paclitaxel   | TAXOL INJECTION 30 mg | AAV8329 | P50J | $-2.97$ (-2.97 to -3.96) | ◯ | Bristol-Myers Squibb Company (Tokyo) |
|              | Paclitaxel Inj. 100 mg/16.7 mL “NK” | 965430 | P50J | $-4.95$ (-3.96 to -4.95) | ◯ | Nippon Kayaku Co., Ltd. (Tokyo) |
|              | *Paclitaxel Inj. 30 mg/5 mL “NK” | 961970 | P50J | $-4.95$ (-4.00 to -5.00) | ◯ | Nippon Kayaku Co., Ltd. (Tokyo) |
|              | *Paclitaxel I.V. Infusion 100 mg/16.7 mL Hospira | D096874AA | P50J | $-3.96$ (-3.96 to -4.95) | ◯ | Pfizer Japan Inc. (Tokyo) |
|              | Paclitaxel I.V. Infusion 30 mg/5 mL Hospira | D016875AA | P50J | $-3.96$ (-3.96 to -4.95) | ◯ | Pfizer Japan Inc. (Tokyo) |
| Pemetrexed sodium hydrate | Alimta Injection 100 mg | C558076AA | P50J | $-2.97$ (-2.97 to -3.96) | ◯ | Eli Lilly Japan K.K. (Kobe) |
|              | Alimta Injection 500 mg | C566187AA | P50J | $-2.97$ (-0.99 to -2.97) | ◯ | Eli Lilly Japan K.K. (Kobe) |
| Ramucirumab  | *Cyramza Injection 100 mg | C435648AF | P50J | $-3.96$ (-2.97 to -4.95) | ◯ | Eli Lilly Japan K.K. (Kobe) |
|              | Cyramza Injection 500 mg | C435647CC | P50J | $-3.96$ (-2.97 to -4.00) | ◯ | Eli Lilly Japan K.K. (Kobe) |
| Vindesine sulfate | Fildesin 1 mg | 4045 | P14J | $-1.98$ (-1.98 to -2.00) | ◯ | Nichi-Iko Pharmaceutical Co., Ltd. (Tokyo) |
| Vinorelbine ditartrate | Navelbine Injection 10 | 505AEI | P14J | $-4.95$ (-2.97 to -4.95) | ◯ | Kyowa Kirin Co., Ltd. (Tokyo) |
|              | Navelbine Injection 40 | 137AEG | P14J | $-4.95$ (-3.96 to -4.95) | ◯ | Kyowa Kirin Co., Ltd. (Tokyo) |

* n = 4 due to damage to the protector.
We created a database of compatibility between 71 drugs and protectors. This database is considered to be the basis for exposure control of hazardous drugs when considering the use of the BD PhaSeal™ System CSTD.

In this study, we used only the BD PhaSeal™ protector, which is the most commonly used protector in Japan, and our method has not been used to assess other CSTDs. Because this method pressurizes the inside of the pressure test equipment at 100 kPa, it is unsuitable for instruments using filters. Furthermore, may be difficult to adapt the method to equipment that cannot be equipped with a pressure gauge.

**CONCLUSION**

The database created in this study comprises data from objective measurements of the presence or absence of leakage of anticancer drugs when using the BD PhaSeal™ System CSTD, and these data may form the basis for the use of this CSTD in exposure control when preparing anticancer drugs.

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**Conflicts of Interest**  Hiromasa Ishimaru received drugs from Nichi-Iko Pharmaceutical Co., Ltd., Eli Lilly Japan K.K., Mochida Pharmaceutical Co., Ltd., Kyowa Kirin Co., Ltd., Nippon Kayaku Co., Ltd., Sawai Pharmaceutical Co., Ltd., Shionogi & Co., Ltd., Towa Pharmaceutical Co., Ltd. and Yakult Honsha Co., Ltd. The remaining authors declare no conflicts of interest.

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