Hazardous drugs
NIOSH has defined hazardous drugs as those with six characteristics (e.g., teratogenicity, carcinogenicity or reproductive toxicity) observed in humans or animals. Hazardous drugs are recommended to be prepared in biological safety cabinet (BSC) and healthcare workers need safe handling skills.

5-Fluorouracil (5-FU)
Antineoplastic drugs account for most of the hazardous drugs. Among them, 5-FU is a common cytotoxic antineoplastic drug, and can potentially cause harm if not handled properly.

Material and Methods

5-FU contamination
During preparation, 5-FU contamination on 2 stainless steel plates (10 cm × 10 cm) in the BSC was determined. These stainless steel plates were collected at the end of the protocol period.

Measurement
We sampled 5-FU from these 2 plates with 40 mL of 90% acetonitrile in water. Samples were analyzed by a validated liquid chromatography coupled to tandem mass spectrometry method. Limit of quantitation is 1 ng/mL.

Diurnal variation
Relative standard deviation (%CV)

<table>
<thead>
<tr>
<th>Component</th>
<th>Relative standard deviation (%CV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of plate placement in the BSC</td>
<td></td>
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</tbody>
</table>

Analysis
We examined the correlation between 5-FU contamination level and the following four items:

1. Amount of 5-FU prepared
2. Time of plate placement in the BSC
3. Operator’s experience in mixing
4. Number of anticancer agents prepared at each hospital

Results

Table 2. Characteristics of objective items
<table>
<thead>
<tr>
<th>Participating institution</th>
<th>Average</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 national hospitals in Japan</td>
<td>16 pharmacists</td>
<td></td>
</tr>
<tr>
<td>13 vials</td>
<td>2 – 38 vials</td>
<td></td>
</tr>
<tr>
<td>1.71 hours</td>
<td>0.1 – 5.5 hours</td>
<td></td>
</tr>
<tr>
<td>35 months</td>
<td>1 - 168 months</td>
<td></td>
</tr>
<tr>
<td>1427</td>
<td>326 - 4500</td>
<td></td>
</tr>
</tbody>
</table>

Discussion
There were 5 pharmacists with 5-FU contamination at the level less than detection limit. Importantly, years of preparation experience varied among these pharmacists. These results suggested that even experienced pharmacists may underestimate the risk of environmental exposure and/or overestimate mixing skills during normal preparation. The routine training of mixing skills is needed to safely handle anticancer agents.

Conclusions
These results suggest no relationship among the level of 5-FU contamination during normal mixing, the time of plate placement in the BSC, the operator’s experience in mixing, the amount of 5-FU vial prepared, and the number of anticancer agents prepared at each hospital.

Acknowledgements
We would like to thank Dr. S. Hamamichi for useful advice on this poster, and pharmacists who participated in this project. We have no conflict of interest to disclose.