



*Is it time for more precise legislation on exposure to hazardous drugs?*

A MindMetre Research Note – February 2017

This short research note is designed to highlight the issue of nurses who administer cytotoxic chemotherapy drugs being exposed to – and damaged by – the harmful effect of these drugs. We look at a number of recent pieces of evidence emerging in Europe, and raise the question as to whether official guidelines should be interpreted more rigorously, and specific legislation introduced, in order to better protect dedicated oncology nurses from sustaining long-term damage in the course of their work – a situation which is clearly morally unacceptable.

## **Anecdotal evidence that oncology nurses are insufficiently protected**

MindMetre, which regularly addresses and researches patient safety and healthcare worker safety issues across Europe, has examined anecdotal evidence that harm is being sustained by chemotherapy nurses in UK NHS Trusts, most probably as a result of exposure to the hazardous cytotoxic drugs they are handling in their day-to-day duties. Although this evidence is at present purely anecdotal, and cannot be regarded as quantitative, the fact that harm from occupational exposure is being reported at all would suggest that this area of healthcare worker safety merits further investigation, as well as better standards of healthcare worker protection. A number of robust studies from around the USA and Europe have confirmed harm is being sustained from such exposure<sup>1,2,3,4</sup>. To quote one recent study<sup>5</sup>, “the occupational risks to health care workers handling these drugs in the course of their duties still need to be fully addressed.”

The testimony of chemotherapy nurses up and down the UK, that has been examined by MindMetre, includes a range of symptoms. In Yorkshire, three nurses reported significant hair loss since working in the oncology specialism. In the West Midlands, nurses reported flu-like symptoms when a particular anti-neoplastic drug was being administered to patients, along with the disappearance of these symptoms when the treatment course ended. In the North West an unusually high incidence of miscarriages among chemotherapy nurses was noted, paralleled by similar reports from East Anglia, Humberside, the South West and the Midlands.

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## An investigation in Spain

These anecdotal reports of ill-health among chemotherapy nurses are too pronounced to be mere coincidence, and – at least if replicated across the country – bear the hallmarks of conditions resulting from exposure to hazardous drugs. Given that there is no significant difference between European countries in terms of oncology nurse occupational protection standards, we might assume that the situation is likely to be similar across the other main economies of Europe – Germany, France, Italy and Spain. Certainly, the increased risk of nurses in oncology departments sustaining damage from cancer treatments is well documented in the clinical literature<sup>6</sup>.

Interestingly, Spain is precisely where an investigation last year by the official prosecutor has brought the issue into high relief. The investigation, which examined staff and union complaints about nurse exposure to (and damage from) cytotoxic drugs, imposed a mandatory increase in standards of preparation and **administration** of these hazardous substances<sup>7</sup>. Reporting on the investigation noted that “If the Prosecution Office can prove that, as the nursing team claims, the handling of cytostatic medicines is not carried out properly due to malpractice and negligence by hospital management, the issue could have serious legal repercussions<sup>8</sup>.” Furthermore, the investi-



gation uncovered levels of contamination of which the hospital may have been genuinely unaware. Reporting at the time noted that “Technicians... were able to verify the presence of cytotoxics on work surfaces, in the air or in the urine of exposed persons. In relation to the possible adverse effects that chronic occupational exposure to low levels of concentration of compounds with cytotoxics can cause, [the investigation] warns that these effects ‘may be subclinical and not be obvious for years or generations of continuous exposure<sup>9</sup>.’”

The legal process around this case is ongoing. One member of staff has been awarded compensation for damage sustained from exposure to cytotoxic drugs<sup>10</sup>. However, it is noteworthy that radically improved systems have been introduced to protect healthcare workers right across the cytotoxic drug preparation and administration cycle. In particular, the hospital now uses Closed System Transfer Devices (see next section) that completely eliminate any escape of cytotoxic drugs, and has introduced measures in pharmacy and ward that reduce contamination rates to virtually zero, thereby better protecting care staff. Similarly significant contamination rate reduction has been corroborated in other clinical studies<sup>11</sup>.



## Academic voices and closed systems definitions

Academic voices in the UK have also taken up the issue<sup>12,13</sup>. An important paper from senior lecturers at the University of Birmingham summarises the evidence for occupational exposure and harm, and identifies more widespread use of ‘closed transfer systems’ as a key measure to protect oncology nurses at work. Closed System Transfer Devices (CSTDs) are defined by the U.S. National Institute for Occupational Safety and Health (NIOSH) as “a drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system.” (NIOSH 2004: 44)

NIOSH has clarified its definition further<sup>15</sup>:  
*“In regards to [the] question on what NIOSH considers to be a closed-system transfer device (CSTD... the intended function was to preserve the sterility of the product while preventing the escape of a hazardous drug, in whatever form it may exist, into the surrounding environment. In that regard, if a hypothetical CSTD was successful in meeting these performance criteria during the drug transfers for which it was intended, we would probably consider it as meeting the definition. If however, the hazardous drug under manipulation included a vapor component or could change phase to vapor during the drug transfer process, leading to escape of drug from the system, then that system would fail to meet the intended function of our definition.”*

The U.S. official definition of a CSTD is important because official guidance<sup>16</sup> published by the Spanish National Institute of Safety and

Hygiene at Work (INSHT) specifically refer to the NIOSH definition as an equivalent to the required national standard. The Spanish official guidance<sup>17</sup> goes on to say that “Devices for access to both the primary receptacle and the other receptacle, and the connection to the application bags, must **eliminate the phenomenon of aerosolization** through pressure equalisation or equivalent mechanisms.” No wonder, then, that the Birmingham University paper’s authors categorically state that “In order for CSTD to be used to their full potential and maximise reduction in exposure of healthcare workers to hazardous substances, CSTD should be used across the whole drug journey from reconstitution to administration and disposal<sup>18</sup>.”

Official guidance from the Health Authorities in other European countries has not yet defined the requirements of truly closed systems quite so closely as in Spain. Some, however, do reference the NIOSH guidelines<sup>19</sup>. However, given growing awareness of the issue (there is even a public petition to Government and Parliament currently live in the UK to “Make the use of closed systems to administer anticancer drugs (chemo) compulsory<sup>20</sup>”), such clarification is likely to spread across Europe at the national level in the near future. In the UK, the Health and Safety Executive already uses a superlative in its guidance to “Use totally enclosed systems where reasonably practicable<sup>21</sup>.” In other European countries, the official guidance phrases are close to the UK definition and tend to reference the US standard<sup>22</sup>.

## Is measurement insufficiently rigorous?

The testimony evidence examined by MindMetre would tend to indicate that contamination levels between pharmacy and point of administration are not always regularly or thoroughly investigated. The absence of consistently collected evidence in the cytotoxic drug administration trail in a majority of hospitals, combined with persistent financial pressure on healthcare systems across Europe, may well have led to a tendency not to investigate contamination too closely. Yet it is precisely that administration procedure that tends to lead to greatest risk of exposure, with current standard bag and spike methods opening the door to regular contaminant escape through spillage or aerosolization. One recent paper on the subject notes that, “the interior of isolators and the contents thereof (e.g. infusion bags and syringes) are readily contaminated by aerosols and spillages and afford a secondary source of exposure to pharmacists, nurses and cleaning staff. Closed system transfer devices (CSTDs), designed to prohibit the transfer of contaminants into the working environment during drug transfer between the vial and syringe, have been successful in further reducing, but not eliminating surface contamination. Given that

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the number of patients requiring treatment with chemotherapeutic agents is predicted to increase, further efforts to reduce occupational exposure to anti-cancer drugs, including the refinement and wider use of CSTDs, are recommended<sup>23</sup>.” Anecdotal evidence seen by MindMetre tends to corroborate the efficacy of CSTDs in reducing the effects of exposure, with one oncology department in the South East of England reporting that skin and respiratory problems among specialist nurses experienced during drug preparation disappeared during a CSTD trial.

## Recommendations at the European level

Now the issue of oncology nurse exposure has reached the European stage, with the publication of *Preventing occupational exposure to cytotoxic and other hazardous drugs, European Policy Recommendations*<sup>24</sup>, launched in the European Parliament on 26 April 2016. The paper notes that although the increasing risk has been widely recognised across Europe – including bodies such as the European Agency for Safety and Health at work, there is not yet any specific legislation, guidelines or minimum standards which precisely defines processes in EU member states on handling cytotoxic drugs. Nevertheless, in November 2015, the European Parliament did call on the Commission to take action on this issue. This new paper launched in April calls for legislation to be put in place, and

includes a specific recommendation on CSTDs which is very much in line with the recommendations from the University of Birmingham paper cited earlier in this research note.

The European Policy Recommendations state, in their seventh recommendation, that “European legislation should establish a common definition for Closed-System Drug Transfer Devices (CSTDs, which details the technical specifications to be met by a medication transfer system to be considered as a closed system, using the definitions established by the National Institute of Occupational Safety and Health (NIOSH)... Harmonised protocols for testing CSTD should be established<sup>25</sup>.”

## Conclusions

In conclusion, MindMetre is of the opinion that a rising body of commentators – clinicians, academics and policymakers – are recognising the hazardous drug exposure risk for oncology nurses. While healthcare worker protection is well governed during the preparation of these drugs, it would appear that exposure risk is not yet properly mitigated throughout administration procedures. With healthcare systems throughout Europe under severe financial pressure, specific legislation is required to empower embattled pharmacy and clinical services heads to insist on implementing robust safety measures from preparation to administration, including tightly defined closed-systems, and mandatory surveillance of contamination levels outside of pharmacy preparation.

MindMetre will be continuing to monitor the emerging situation. As with other healthcare worker safety legislation, it is a matter of principle that staff should be protected as far as is possible in the course of their work.



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1. Turci R, Sottani C, Ronchi A, et al. Biological monitoring of hospital personnel occupationally exposed to antineoplastic agents. *Toxicol Lett* 2002; 134: 57–64.
2. Cornetta T, Padua L, Testa A, et al. Molecular biomonitoring of a population of nurses handling antineoplastic drugs. *Mutat Res* 2008; 638: 75–82.
3. Fransman W, Hillhorst S, Roeleveld N, et al. A pooled analysis to study trends in exposure to antineoplastic drugs among nurses. *Ann Occup Hyg* 2007; 51: 231–239.
4. Sasaki M, Dakeishi M, Hoshi S, et al. Assessment of DNA damage in Japanese nurses handling antineoplastic drugs by comet assay. *J Occup Health* 2008; 50: 7–12.
5. Connor-TH; Eckel-SF; McDiarmid-MA; Polovich-M; Power-AL, Safe handling of hazardous chemotherapy drugs in limited-resource settings, Washington, DC: Pan American Health Organization 2013 Nov; :1-53
6. See, for instance: M. Moretti et al, A study protocol for the evaluation of occupational mutagenic/carcinogenic risks in subjects exposed to antineoplastic drugs: a multicentric project, *BMC Public Health*. 2011; 11: 195; Skov T, Maarup B, Olsen J, Rørth M, Winthereik H, Lynge E., Leukaemia and reproductive outcome among nurses handling antineoplastic drugs. *Br J Ind Med*. 1992 Dec;49(12):855-61; Martin S, Larson E., Chemotherapy-handling practices of outpatient and office-based oncology nurses, *Oncol Nurs Forum*. 2003 Jul-Aug;30(4):575-81.
7. Por Experiencia, CCOO consigue visibilizar los riesgos en la manipulacion de farmacos peligrosos en el Hospital La Fe de Valencia, February 2016
8. El Mundo, Fiscalía mala praxis en La Fe con medicamentos cancerígenos, 16 June 2015
9. El Mundo, Trabajo exige a La Fe que cambio el uso de fármacos cancerígenos, 22 June 2015
10. Por Experiencia, CCOO consigue visibilizar los riesgos en la manipulacion de farmacos peligrosos en el Hospital La Fe de Valencia, February 2016
11. Simon N, Vasseur M, Pinturaud M, Soichot M, Richeval C, Humbert L, et al. (2016) Effectiveness of a Closed-System Transfer Device in Reducing Surface Contamination in a New Antineoplastic Drug-Compounding Unit: A Prospective, Controlled, Parallel Study. *PLoS ONE* 11(7): e0159052. doi:10.1371/journal.pone.0159052
12. N Vyas, A Turner, JM Clark, GJ Sewell, Evaluation of a closed-system cytotoxic transfer device in a pharmaceutical isolator, *Journal of Oncology Pharmacy Practice*, 2014
13. GJ Sewell, Essential control measures in cytotoxic practice, *Hospital Pharmacy Europe*, 2015
14. *British Journal of Nursing* Vol.24 No.14, A Simons & S Tolund, Closed systems for drug delivery: a necessity not an option, 2015
15. Letter to Carmel Pharma ab (Göteborg, Sweden) (Thomas H. Connor, NIOSH Cincinnati, personal communication), cited in *Annals of Occupational Hygiene*, NIOSH definition of closed-system drug-transfer devices, 27 May 2009, *Ann Occup Hyg*. 2009 Jul; 53(5): 549
16. National Institute of Safety and Hygiene at Work, Technical Prevention Notes, Occupational exposure to cytostatic compounds: safe systems for their preparation, 2015
17. Nota Técnica de Prevención (NTP) 1051
18. *British Journal of Nursing* Vol.24 No.14, A Simons & S Tolund, Closed systems for drug delivery: a necessity not an option, 2015
19. For instance: Royal Pharmaceutical Society, Quality Assurance of Aseptic Preparation Services – Standards, 2016, “CLOSED SYSTEM TRANSFER DEVICE A drug transfer device that mechanically prohibits the transfer of environmental contamination into the system and the escape of hazardous drug or vapour concentrations outside the system. (NIOSH Alert 2004).”
20. <https://petition.parliament.uk/petitions/123762>
21. HSE, Safe handling of cytotoxic drugs in the workplace
22. For example: <http://www.aip-marseille.org/wp-content/uploads/2015/06/Cours-Oncologie-DM-en-oncologie.pdf>
23. *Journal of Oncology Pharmacy Practice*, N.Vyas, G.Yiannakis,A.Turner, G.J.Sewell, Occupational exposure to anti-cancer drugs: A review of effects of new technology, *J Oncol Pharm Practice* 2014 Vol 20(4) 278-287
24. [http://www.europeanbiosafetynetwork.eu/Exposure%20to%20Cytotoxic%20Drugs\\_Recommendation\\_DINA4\\_10-03-16.pdf](http://www.europeanbiosafetynetwork.eu/Exposure%20to%20Cytotoxic%20Drugs_Recommendation_DINA4_10-03-16.pdf)
25. Ibid