ROUND TABLE

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Closed System Transfer Devices for the preparation of hazardous drugs – the European perspective

hospital pharmacy europe


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The preparation, handling and administration of hazardous drugs pose considerable risk to healthcare professionals, and yet the uptake of closed system transfer devices in Europe remains low. Why? A group of senior hospital pharmacists from the UK, Germany and France met recently to share perspective on the risks of contamination, the barriers to adoption of CSTDs, and where there are opportunities for their uptake

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The utilisation of closed system transfer devices (CSTDs) is estimated globally to be 12%, almost all of which is in the preparation of cytotoxics and hazardous drugs. In Europe, it is even less that that - it is estimated that fewer than one in ten preparations are made using a CSTD.

If it is the case that CSTDs lower the risk of contamination, and that the health and safety of healthcare workers is of paramount importance, then it follows that a clear understanding of the barriers to uptake needs to be gained.

Risk

Where is the risk, and who is vulnerable?

Risk of contamination with hazardous drugs is present in their preparation and in their administration, wherever they occur, for whoever is handling.
The level of risk is currently measured by monitoring the level of contamination in the environment in which the preparation is done: in the UK, there are mandatory reviews on the environment; in France, as in Germany, monitoring is annual (but not mandatory) and after each leakage.

Key to the risk concept is understanding the relative and absolute risk of a procedure, and to minimise any impact on the healthcare worker.

Still on the issue of site of risk, there is real concern over pharmacists' perception that, once risk is mitigated at preparation by procedures and processes in which the healthcare workers are well trained, and usually in centralised, controlled environments, risk of contamination has been mitigated.

Pharmacists may develop a blind spot for the perhaps even greater risk at the point of administration, whether that occurs on the ward or on the 'virtual ward' of the community (as more healthcare is pushed into the community), in the hands of healthcare workers who may be less well trained in safety procedures that would protect them and their patients. In a sense, moves to dose-banded cytotoxics and automation further remove the pharmacist from the perception of risk in the overarching process of hazardous drug usage.

The issue of drug management is critical in the consideration of CSTD uptake, and there seems to be confusion regarding what is known of the quantifiable risks and the safety-added value of CSTDs, that would be needed to outweigh the counter arguments of added cost in terms of unit price, training and preparation time.

What price safety? Perhaps what suffices is to be able to cite studies that show that there is less contamination using CSTDs than not: they are safer than the status quo, even if not 100% safe. And if healthcare workers are safer, less likely to be contaminated by highly hazardous drugs, then mitigation becomes a matter of duty of care of the employer. If safety comes first, albeit at a price, the uptake of techniques and devices that provide safety is rational, if at odds with budget holders.

Shelf life considerations

It is the professional responsibility of every pharmacist to ensure that the drugs from his pharmacy are safe, sterile and stable.

CSTDs can also be useful for extending shelf life. For those situations in which shelf life beyond that stated in the Summary of Product Characteristics (SPC) is required, in Europe the two major sources of extended stability data are Stabilis® and the Krämer list. The former is a collection and analysis of all literature published on the matter, including levels of recommendation (against a checklist of attributes) and sources of literature, and is considered to be a very strong, reliable source. The Krämer list is also a highly reliable

'There is inter-operator variability: what gets done in a unit is just one step in a process'

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source, although, like Stabilis®, it does not provide the parameters and specifications of the methods underpinning the studies.
Whichever source is used, there may be specific conditions under which the drug is being prepared and stored that require that the pharmacist conduct his own analysis.

In the UK, shelf life is also regulated by whether or not the pharmacist works in a Medicines and Healthcare Products Regulatory Agency (MHRA)-licensed unit: a licensed unit will be providing batch-produced product for internal as well as external use, and the driver is to verify as long a shelf life as possible, whereas product prepared in a unit that is not MHRA licensed will have a shelf life of seven days maximum.

The acceptable level of degradation product and toxicity of leachables from storage/preparation containers are complex issues of major importance in assessing a product's shelf life, and are the subject of ongoing research.

Barriers

First and foremost of the barriers to uptake of CSTDs is the perception of some pharmacists that the *status quo is safe enough* – that CSTDs show no evidence of a decrease in contamination. So there is no need to do things differently: the barrier of inertia.

In any case, there may be the position, as held by some German pharmacists, that *there is no such thing as a truly closed system*. So there can be no safety advantage, in or out, in any case.

If thinking extends beyond this stage, there comes the barrier around *remuneration* or paying for medicines. In the UK, high-cost items are paid for by the Clinical Commissioning Group, but the cost of CSTDs would come out of a fixed consumables budget.
So even if the argument in favour of uptake of CSTDs is made, say, in the case of ward nurses – which is difficult, given the difficulty not to mention the cost of measurement – the money to pay for it still has to come from that fixed budget.

'The UK Health & Safety Executive recommends the use of totally closed systems where reasonably practicable, to control exposure to cytotoxic drugs'

Key points

- **The definition of CSTD used in this report is that agreed by the National Institute for Occupational Safety and Health (NIOSH) and the International Society of Oncology Pharmacy Practitioners (ISOPP), who define a closed system drug transfer device to be 'a drug-transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapour concentrations outside the system'.**
- **Risk of contamination with hazardous drugs presents itself at the sites of preparation and administration:**
  - **While preparation of cytotoxic drugs is performed in controlled centralised facilities, by appropriately trained healthcare professionals, that is not necessarily the case for other hazardous drugs, for example antibiotics and monoclonal antibodies (mAbs).**
  - **Neither is it the case for the administration of hazardous drugs, which will occur on the ward, not necessarily in the hands of healthcare professionals with the necessary training and skills.**
- **Because there is no indicator for risk measurement, it is difficult to argue the safety added value of a CSTD, such that it outweighs the time and cost of its adoption.**
- **While there will always be a call for additional clinical data in support of a decision to adopt CSTDs, what is more highly valued is its ease of use in the hands of nurses as well as pharmacists and pharmacy technicians, for which sustained training support is ideal.**
- **If a CSTD is shown to reduce contamination, the employer has a duty of care to take it into consideration in ensuring the safety of his employees. To that end, occupational health guidance may prove to be the key driver behind the uptake of CSTDs.**
- **The adoption of CSTDs is at odds with that of dose banding, whose automation is incompatible with CSTDs, and with batch production, which will most cost-effectively rely on automation.**

Chief Pharmacists have to make hard budgetary decisions at the macro level, not at the micro level. CSTDs will be bought at the expense of some other item.

In the *absence of a mandate* at national or EU level, for example, a positive NICE Technology Appraisal, there is no clearing the cost hurdle.

Regional and national agencies are ambiguous in their recommendations for the handling of hazardous drugs, leaving decisions to be made at the hospital level. One example of this the EU Sharps Directive (Directive 2010/32/EU – Prevention from sharps injuries in the hospital and healthcare sector). Should it ever be adopted across Europe (it was to have been integrated into national legislation in 2013), there would be repercussions in terms of the choice of CSTD.

A major barrier to CSTD uptake has been touched upon above in discussing *risk perception*. When, as is the case in the UK, nearly 100% of preparations are now done centrally by highly trained personnel in highly controlled settings, it is perceived that the risk has been mitigated. So even if CSTDs have been used in the preparation phase of the process, there is no perceived need for similar standards of care to be used in the location of administration.

Following on from this, in the UK, nearly 5% of cytotoxics are bought in dose banded, and this is starting to be the trend (although lagging) across Europe.

One issue concerning *dose banding* is the uncertainty of any impact it will have on the uptake of CSTDs, for the reason that risk (ie. preparation risk) has been migrated. The other barrier presented by dose banding is that the *automation* that drives it is incompatible with CSTDs – which will win the race, dose banding or CSTDs?

The *perceived lack of suitable clinical data* proving improved safety is used as a barrier for uptake of CSTDs. But a more critical barrier is a device that is *not easy to use, and for which there is not a continuous and practical training programme*. If a device is not easy to use (which will come with appropriate, sustained training), it will not be used. If asked to choose between two CSTDs – one very easy to use that results in a clinically proven 95% reduction in contamination, and one resulting in 100% reduction in contamination but cumbersome – it is the former that will be bought.

'The UK is very focused on antimicrobial stewardship: here is a real opportunity to introduce CSTDs into practice'

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Key opportunities

The key opportunities for increasing the use of CSTDs in Europe as identified by the group of delegates are here illustrated, pinpointing the focus on expanding the use of CSTDs for the preparation and administration of all hazardous drugs.

The 'existing uses' is defined as preparation of cytotoxics by trained pharmacists/pharmacy technicians in centralised, controlled facilities.

The 'new uses' is defined as (1) the administration of cytotoxics by nurses on the ward; (2) the preparation of non-cytotoxic hazardous drugs (eg. mAbs, antibiotics) by trained pharmacists/pharmacy technicians in centralised, controlled facilities; and (3) the administration of non-cytotoxic hazardous drugs by nurses on the ward.

	EXISTING PRODUCT/SERVICE	NEW PRODUCT/SERVICE
EXISTING USES	• Published evidence of reduction of contamination • Challenge perception that the system is not closed • Proof of improved sterility to support argument for cost savings from decreased waste • Focus on ease of use as critical driver • Consider NICE Technology Appraisal	• Needle-free system • Improve ease of use, as seen to be key driver for uptake • Automation compatibility
NEW USES	• Antimicrobial stewardship • Training and competencies support • Use HSE recommendation to drive to nurse acceptance • Virtual wards – push into the community	• Partnership approach: the service support becomes the added-value product

Opportunities

- **Mitigate risk of contamination at the administration phase, ie. on the wards, and in the community, when in the hands of nurses**
- **Emphasise ease of use of the system, backed up with training and competences support**
- **Extend focus to the preparation and administration of non-cytotoxics hazardous drugs, eg. mAbs and antibiotics**
- **Emphasise trials that show the 'nothing in' superiority of a CSTD maintains the sterility of the product, enabling cost savings of minimum waste from multi-dosage vials**
- **Use the UK HSE recommendation (2015) to advance the argument for the use of closed system transfer devices as a necessary tool in the handling of all hazardous drugs**

Abbreviations

CSTD	**closed system transfer device**
mAb	**monoclonal antibody**
MHRA	**Medicines and Healthcare Products Regulatory Agency**
NICE	**National Institute for Health and Care Excellence**
NIOSH	**National Institute for Occupational Safety and Health**
SPC	**Summary of Product Characteristics**
UK HSE	**UK Health and Safety Executive**

'With essentially 100% of your high-risk medicines prepared centrally, you think you have mitigated risk. You do not think about administration'

Supporting an increase in the use of CSTDs for the preparation of cytotoxic drugs is: (1) the gathering and targeted promotion of clinical data as evidence of a reduction in contamination consequent on the use of CSTDs; (2) a focus on ease of use of a CSTD; (3) consideration of the possibility of applying for a positive NICE Technology Appraisal of the device; (4) challenging the perception that there is no such thing as a closed system; (5) the gathering of proof that CSTD-improved sterility drives cost savings from decreased waste.

Supporting an increase in the use of CSTDs for the preparation and administration of all hazardous drugs is: (1) an understanding of what nurses perceive to be safe levels of risk of contamination in the administration of hazardous drugs, both cytotoxic and non-cytotoxic; (2) promotion of CSTDs hand-in-hand with publicity of the recently released UK Health & Safety Executive (HSE) recommending 'the use of totally closed systems where reasonable practicable, to control exposure to cytotoxic drugs, and potentially extended to all injectable medicines' (Simons A, Toland S. Closed systems for drug delivery: a necessity not an option. *Br J Nursing* 2015;24:S20-S24).

(3) a process-driven programme of training and competences support for nurses; (4) preparation for providing for the safe administration of hazardous drugs in the virtual wards of tomorrow, ie. the community; (5) capitalising on the public health initiatives relating to antimicrobial stewardship.

Should a company choose to look forward to the development of new CSTDs, it could: (1) address the future implementation of the Sharps Directive by developing a needle-free system; (2) develop a system that was ever more intuitive and easy-to-use; and (3) develop a system that was compatible with the automation driving dose-banding and batch production.

Targeting institutions with service elements (training and support) that add value to the decision to adopt CSTDs was considered by the delegates to be of potential value.

Conclusion

There is considerable scope for increasing the use of CSTDs in Europe, given the appetite to fully understand the barriers and embrace the opportunities they offer, the better to challenge the perceptions supporting the status quo.

'The sustainability of our health system is predicated on moving a lot of activity out of hospitals'

Take-home points of recent research into EU adoption of CSTDs (on file, Cogora)

- **It is not generally perceived that CSTDs offer improved sterility compared to current practices, therefore CSTDs must be shown to have advantages relative to use of a needle and syringe, or a spike with filter, in an isolator of biological safety cabinet**
- **The main reason for use of CSTDs is improved staff safety**
- **Because contamination testing is not conducted in at least one-third of hospitals, current staff risk levels may be being underestimated**
- **While cost can prevent hospitals from being able to purchase CSTDs, potential cost-savings achievable by using CSTDs are not a key driver for decisions to buy the devices**
- **This suggests that purchasing of CSTDs for staff safety benefits occurs when there is the budget available**

The roundtable 'Understanding the barriers to EU adoption of CSTDs' was convened in Amsterdam 20 October 2015, with the support of BD, and was attended by Chief Pharmacists from the UK, Germany and France.

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