Preparation of monoclonal antibodies on the pharmacy benchtop – risk assessment and practical considerations

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What was done?

- Preparation of monoclonal antibodies (mAbs) on the pharmacy benchtop temporarily introduced in the Pharmacy Aseptic Unit (PAU) of Tallaght University Hospital (TUH).
- Literature review of the hazards associated with handling mAbs – toxicity, immunogenicity, risk reduction measures.
- Guidance from Ireland's National Cancer Control Programme (NCCP)[1] on Pharmacy Benchtop Preparation of mAbs reviewed and implemented.
- Risk assessment carried out for individual mAbs. List of mAbs suitable for benchtop preparation compiled.

Why was it done?

- Significant reduction in production capacity in the PAU in early 2022 for planned repair work.
- mAbs previously considered hazardous if handled by staff[2] – prepared in a dedicated isolator in the PAU in TUH.
- No widely-accepted standards for safe handling of mAbs, although more recent national[1] and international[3,4] guidance allows preparation of some mAbs outside of PAUs once risks appropriately assessed.
- Benchtop preparation of mAbs implemented to maintain patients' treatment regimens and to reduce costs associated with outsourcing.

How was it done?

- Implementation of the NCCP guidance on Pharmacy Benchtop Preparation of mAbs, using the following headings:

1. Risk assessment and Safety:

- Individual mAbs assessed for suitability for benchtop preparation using the Health Service Executive (HSE) risk assessment tool. This considered toxicity, immunogenicity and closed-system-transfer-device (CSTD)-compatibility of mAbs, and Personal Protective Equipment (PPE) required.
- Conjugated antibody-drug complexes deemed unsuitable from a toxicity point of view.[1]
- mAbs of fully murine origin excluded from an immunogenicity point of view[5] (although none are used in TUH).
- mAbs not compatible with the CSTD were not included due to risk of staff exposure.
- PPE required – long-sleeved cuffed gowns, double gloves, FFP2/3 masks and eye protection with side panels.

Risk	Consequence	Actions/Controls/Mitigations	Grade		
			Consequence	Likelihood	Rating
Risk of teratogenicity and/or carcinogenicity due to occupation exposure – medication has potential risk of teratogenicity and carcinogenicity at therapeutic doses in animal models (SPC)	Staff preparing medication suffer adverse effects due to occupational exposure to the medication	Effects at long-term low-dose exposure levels are unquantified and indeterminate Internal exposure risk is moderate via the inhalation and mucosal route, low via the oral route and unlikely possible via the dermal route in the absence of additional controls A closed system transfer device will be utilised during preparation which will reduce potential occupational exposure. All staff involved in preparation have been trained on use of this CSTD Staff involved in the preparation of this medication will wear non-penetrable gown, nitrile gloves, protective mask and eye wear to further limit exposure	This is graded in accordance with the HSE Risk Matrix		
			Major (4)	*Rare/ Remote* (1)	*Low Risk* (4) - *Accept*
Acceptability – The risk is considered acceptable based on the low risk of internalisation of the medication coupled with the use of PPE, CSTD and safe handling precautions					

Figure 1 - Sample HSE risk assessment matrix[1]

2. Equipment and Facilities:

- The CSTD vial adaptor based on air cleaning (filter) technology was replaced with vial adaptor with physical barrier (balloon) – additional safety measure.
- Dedicated area was assigned for benchtop preparation – well-ventilated, clutter-free and easy-to-clean.

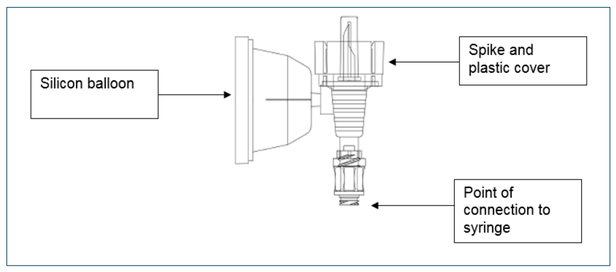

Figure 2 – Diagram of balloon vial adaptor

3. Staffing and Training:

- Presentation given to all PAU staff outlining the risks, and the risk mitigation measures to be put in place. Staff members were satisfied with the changes proposed.
- Additional training on new CSTD vial adaptor was provided by the supplier to pharmacy technicians who were already experienced in aseptic compounding.

4. & 5. Range of Treatments Provided, and Value for Money

- Short shelf-life products unavailable from outsourcing companies were produced on the benchtop.
- Decision to produce some high-cost items on the benchtop to reduce outsourcing costs and potential wastage.

What has been achieved?

- List of mAbs suitable for benchtop preparation prepared. Conjugated antibody-drug complexes, mAbs of fully murine origin and mAbs not CSTD-compatible deemed unsuitable.

Drug	Category	Toxicity information	Antibody type	Compatible with CSTD (06/01/2022)	Advice
Brentuximab vedotin (Adcetris®)	IV Infusion	SPC - No data – risk benefit ratio - Animal studies – reproductive toxicity - Causes testicular toxicity, affects male fertility	Antibody-drug conjugate	Yes	Continue to compound in negative pressure isolator
Cetuximab (Erbitux®)	IV Infusion	SPC - No human data – risk benefit ratio - Animal studies – no increased risk of teratogenicity, however there was a dose-dependent increased risk of abortion	Chimeric	No	Continue to compound in negative pressure isolator
Daratumumab subcutaneous (Darzalex®)	SC injection	SPC - No human or animal data – risk benefit ratio - Human IgG can cross the placenta	Human	Yes	Bench-top preparation possible with closed system transfer device

Figure 3 – Excerpt from list of mAbs suitable for benchtop preparation

- mAbs prepared on the benchtop during period of reduced capacity, facilitated through risk assessment and risk reduction using PPE, training and CSTDs.
- Patients' treatment regimens maintained, and outsourcing costs and wastage reduced.
- The rollout took approximately 30 hours' work over an eight-week period to implement.

What next?

- Contingency plan for benchtop preparation of mAbs in case of reduced compounding capacity in the future.
- NCCP guidance applicable to other organisations experiencing periods of reduced capacity, although it is time-consuming to implement.

References:

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