

# MONOCLONAL ANTIBODIES

*National Centralised Intravenous Additives Service (CIVAS) group and British Oncology Pharmacy Association (BOPA) joint statement on the handling of monoclonal antibodies*

**M**onoclonal antibodies are prominent among the new types of therapeutic agents currently being introduced into clinical practice. These differ chemically and pharmacologically from the small molecules that have traditionally been used as drugs. Therefore, careful consideration needs to be given to their handling, to ensure the safety of staff and patients, and the preservation of product efficacy up to the point of patient administration.

This statement has been produced because local practice regarding monoclonal antibodies varies significantly and there is little specific research on which to base good practice. Some local guidance documents offer advice which is not evidence-based and seems neither logical nor practical. Therefore, the committees of the BOPA and CIVAS groups felt that it would be appropriate and helpful to the members of their organisations to issue a joint statement on this subject.

In doing so, the lack of specific research in this area is acknowledged and the pragmatic nature of this document is based on an understanding of the chemical and pharmacological nature of the products involved.

The characteristics of therapeutic antibodies will depend on both their source and therapeutic target.

Monoclonal antibodies for therapeutic use are produced in tissue culture by antibody-producing cell lines. In the past, the antibodies have been of the type produced by the species in which they were first raised, ie, they were usually murine. However, most antibodies entering clinical practice or under development have been "humanised", so that in the final product only the antigen recognition site corresponds with the original murine.

Humanised antibodies have a very low immunogenic potential. Although genetic engineering techniques are used to produce humanised antibodies, those in current use are not designed to interact directly with the recipients genetic material, that is, they are not gene therapy products.

Monoclonal antibodies can be raised for almost any biochemical or cellular target. Some lead to the death of target cells. However, they are not conventional cytotoxic drugs. They do not interact directly with the translation or transcription of DNA or RNA and would not be expected to be mutagenic or teratogenic. Animal tests support this supposition.

Potential hazards of the products and how to handle them are shown in the table.

Although it is important to consider the specific problems related to any new product, there is no reason, at present, why therapeutic antibodies should not be prepared in the same aseptic facilities used for other types of products. Where these antibodies are intended for the treatment of

malignancy, these include facilities normally used for the preparation of cytotoxic chemotherapy.

*This statement, which was prepared in May 2001 by Max Summerhayes and Richard Needle, has been approved jointly by the committee members of BOPA and the CIVAS Group. It will be reviewed as new evidence becomes available but not later than May 2003.*

*Table: Potential hazards and recommendations for handling*

## Potential hazard

## Recommendation

### Allergic reactions

#### *Non-humanised antibodies*

Allergic sensitisation is a risk with antibodies of non-human origin. This might be expected to be a particular problem with murine antibodies, given the high level of sensitisation to murine proteins seen in people working with rodents.

Since the risk of staff becoming sensitised to these products is greater than for humanised antibodies, the argument for centralised preparation within the controlled environment of a pharmacy compounding unit is stronger than for other types. Otherwise the next statement on humanised antibodies also applies to non-humanised antibodies.

#### *Humanised antibodies*

These are, essentially, human proteins and the risk of an allergic reaction is probably no higher than it is to any of the myriad of other drugs handled in pharmacy units.

As a class, these do not require specific facilities for their safe handling since they pose no special risk to the operator or the environment. Therefore, they can be handled in the same facilities as those for other aseptic products.

### Other exposure hazards

#### *Antibodies currently used as anticancer agents*

Those currently approved for clinical use do not interfere directly with nucleic acid synthesis or function. Therefore, they would not be expected to have carcinogenic or teratogenic effects. Such effects have not been observed in laboratory studies. Thus, although these drugs represent a new therapeutic class that should be viewed with sensible caution, those currently approved present no obvious hazards to staff. This is reflected in the lack of special handling precautions recommended by their manufacturers.

Those presently used routinely do not appear to be carcinogenic or teratogenic and so they can be handled in the same facilities used for non-cytotoxic aseptic products. It is our view that, when being used for the treatment of malignancy, they can also be manipulated in facilities normally dedicated to the manipulation of conventional cytotoxic agents. We consider that the risks of cross-contamination of antibodies by cytotoxic agents or vice versa are small and likely to be of no more clinical significance than the equally rare occurrence of cross contamination between different cytotoxic agents handled within the same facility.

#### *Other antibodies used therapeutically*

Other antibodies should be considered on the basis of what is known about their pharmacology, but there is no reason to suppose that this group of agents is, as a class, likely to pose any particular hazard to those handling them.