Sharp and to the Point: developing needles for high throughput and critical compound administration in mice

Overall aim

To develop a device that enables injections in mice without losing material to dead space, allows needles to be changed quickly and safely between animals to ensure sharpness and sterility, and which prevents cross-contamination between animals. This must be competitively priced to facilitate broad uptake across the bioscience sector.

Duration

Up to one year

Budget

Up to £100k

Sponsor(s)

AstraZeneca, GSK, The Royal Veterinary College London, The University of Sheffield

Background

Hypodermic needles are used throughout medical research involving animals for injecting substances (e.g. via intravenous, subcutaneous, intraperitoneal or intramuscular routes) or for collecting blood samples. Most needles used to administer material parenterally in animals are designed and sold as single-use disposable needles.

Where needles are re-used, it is commonly done to reduce time and cost because of the involvement of large numbers of mice and/or test material. Two blogs published on the NC3Rs website have focused on the topic of re-using hypodermic needles in day-to-day practice and highlight the associated scientific and welfare concerns [1,2].

The re-use of needles results in a loss of sterility and can increase the risk of infection and disease transmission between individual animals and between cages. Re-use also risks dulling of the needle, potentially increasing the pain and discomfort associated with subsequent injections. These concerns create confounding and unnecessary variables which can impact the quality of scientific data collected.

When needles are re-used in mouse studies, it is most often to address the following:

- **Loss of material to dead space**. The primary reason for re-use of needles and syringes is loss of valuable material (such as cells, compounds, viruses) in the fluid not expelled due to dead space between the syringe and the needle hub. The materials used in pilot studies are often difficult and expensive to synthesise and are therefore made in small quantities. This, combined with the size of mice and the small volumes administered, mean dead space losses can form a significant percentage of the material needed. An increasing number of studies involve the injection of living cells for example, for xenograft models used in oncology research. To account for dead space losses during administration, an excess of cells is needed. For certain cell lines, these can be difficult to grow and harvest in large quantities without affecting their quality.

- **The time needed to change needles between injections**. This can be a concern for studies where materials may need to be injected within a limited time into large numbers of animals. For example, changing the needle for each animal in a study where the formulation stability requires all animals to be dosed within an hour of formulation preparation would require additional staff to complete the injections within the necessary timeframe.

It is possible to purchase low dead space needles and syringes. However, they are not available in all needle gauges, and the syringe barrels are often difficult to read for small volumes which can affect the accuracy of small volumes draws. Insulin syringes have been developed that have no dead space. However, these are supplied with the needle attached making them inappropriate for use with substances that cannot be drawn up through the needle (e.g. cells).

All currently available products require significant time to manually change a needle between each animal.

3Rs benefits

There is evidence to show that the single use of a needle can cause significant dulling/deformity of the needle tip [1], and that re-use of these needles may cause transient pain [3,4] and tissue damage at the site of injection. The transfer of material between animals (blood/tissue) can also increase the risk of infection and cross-contamination between cages of mice may occur. Infection and disease transmission can lead to study failure and result in further animal use and welfare concerns as well as loss of time and money. Use of needles more than once can also affect the quality of the scientific data collected as each animal in the cage is treated differently with respect to the process of injection.

In 2017, 1.89 million animals were used in experimental procedures in the UK. Approximately 58% were mice and many of these would have been involved in procedures involving an injection for example, for basic research programmes, administration of materials in efficacy, toxicity and pharmacokinetic studies, or in vaccine batch testing for quality and safety. A small refinement in how substances are delivered would positively impact a high number of animals.

Key deliverables

Essential

Develop a product that can be used to administer substances parenterally to mice and have the following features:

- Needles must be of suitable quality and sharpness for a single injection through various routes e.g. intravenous, subcutaneous, intramuscular, intraperitoneal.
- Users must be able to rapidly and easily change needles.
- The device must be able to accurately deliver small volumes, typically 0.05 to 0.2ml.
- The device must be able to deliver substances with no loss due to dead space.
- The product must be available with a minimum of three needle gauge in the range 23 to 29G.
- Use of the product must not add a significant amount of time to routine substance administration.

Desirable

- The cost should be comparable to the current costs of standard disposable needles and syringes.

- A sizeable reservoir that facilities studies that require injecting a large number of mice sequentially.
- The ability to adjust the dose between injections.
- To be adaptable to other rodent species.

Sponsor in-kind contributions

The Sponsors will provide:

- Insight into needle usage across a diverse range of settings and applications.
- Expertise and guidance in needle design and compound administration.
- The opportunity to deploy and test the developed product(s) in both industry and academic settings and across different areas including:
    - Oncology
    - Vaccines
    - Basic research
    - Veterinary medicine

References

1. BD Website. *A look at the Reuse of Insulin Needles* [Online] Available at: https://www.bd.com/documents/white-paper/DC_A-Look-at-the-Reuse-of-Insulin-Needles_WP_EN.pdf. [Accessed: 2 July 2019].

2. Robinson S (2019). *Supporting implementation of good practice in animal welfare procedures in a Global Pharmaceutical Company: needle use as an example*, NC3Rs [Online] Available at: https://www.nc3rs.org.uk/news/supporting-implementation-good-practice-animal-welfare-procedures-global-pharmaceutical-company. [Accessed: 2 July 2019].

3. van Gerwen DJ, Dankelman J and van den Dobbelsteen (2012). Needle–tissue interaction forces – A survey. *Medical Engineering and Physics* 34(6):665-80.

4. Whitfield L and Robinson S (2017). *Re-use of needles: is this an indicator of a culture of care?* NC3Rs [Online] Available at: https://www.nc3rs.org.uk/news/re-use-needles-indicator-culture-care. [Accessed: 2 July 2019].