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Comparison of ^{14}C Production Methods and Suitability for Market Needs

Executive summary

One of the tasks (T.5.3.3) of the CARBOWASTE Recycle Work Package is to examine the potential for recycle of ^{14}C. The removal of ^{14}C and opportunities to concentrate this into a form suitable to match the requirements of users/suppliers of ^{14}C, is the subject of report T.5.3.2). This report provides a summary of the discussions to date with the users/suppliers of ^{14}C, the aim of which was to understand their requirements for ^{14}C supply in terms of its purity, concentration and volume. Discussions have been held between the WP5 leaders, a several companies who use and/or supply ^{14}C, currently produced from the by reactor irradiation of nitrogen species. The companies with which discussions have been undertaken are GE Healthcare, ARC Inc and Quotient Bioresearch. The key findings of these discussions, are that:

- The potential industrial recycle of ^{14}C over a number of years could use a significant proportion of the total i-graphite inventory, although it is most unlikely that most or all ^{14}C in irradiated graphite could be recycled.
- Although ^{14}C is produced for manufacturers by reactor irradiation of nitrogen species and hence is available to them in high isotopic purity, the discussions revealed that a lower specific activity (i.e. isotopic dilution) would nevertheless be acceptable to manufacturers as input material for some applications.
- The appropriate choice of graphite (and a "roasted" fraction from it) would allow any isotope separation process to be conducted on a small physical scale, thereby making the process more economic.

Revisions

Rev.	Date	Short description	Author	Internal Review	Task Leader	WP Leader
1	April 11	Final Report	J.C. Goodwin	D. Bradbury	D. Bradbury	D. Bradbury

Contents

Tables

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The key findings of these discussions are that:

- The potential industrial recycle of ^{14}C over a number of years could use a significant proportion of the total i-graphite inventory, although it is most unlikely that most or all ^{14}C in irradiated graphite could be recycled.
- Although ^{14}C is produced for manufacturers by reactor irradiation of nitrogen species and hence is available to them in high isotopic purity, the discussions revealed that a lower specific activity (i.e. isotopic dilution) would nevertheless be acceptable to manufacturers as input material for some applications.
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1 Introduction

One of the tasks (T.5.3.3) of the CARBOWASTE Recycle Work Package is to examine the potential for recycle of ^{14}C. The presence of the isotope ^{14}C is usually considered as a problem in the management of irradiated graphite waste. However, the isotope is used in many applications of chemistry and medicine and is used in quite significant quantities, not grossly dissimilar to the inventory of the isotope in graphite moderated reactors. In order to achieve such recycling two developments would need to take place. First there needs to be an efficient means of separating the ^{14}C from the graphite (see Report 5.3.2), and second the resulting product needs to have the right characteristics of chemical form, isotopic purity and quantity for supply to the market. It also needs to have the right price.

In order to understand both the requirements of suppliers and/or users of ^{14}C, discussions were undertaken between the WP5 leaders and various organisations that use or supply ^{14}C. This report provides an overview of the work undertaken in this area to date, as well as providing a summary of the findings from these discussions, and the conclusions drawn.

2 Results of discussions with ^{14}C suppliers and users

Various suppliers and users of ^{14}C were contacted to discuss their requirements, and to gauge their interest in a potential alternate supply route for ^{14}C as a by product of the decontamination and recycle of irradiated graphite.

2.1 GE Healthcare

GE Healthcare is an arm of General Electric Company and has its headquarters in the UK. They are providers of medical technologies and services to the healthcare sector, with specific expertise in the areas of:

- medical imaging and information technologies,
- medical diagnostics,
- patient monitoring systems,
- performance improvement,
- drug discovery,
- and biopharmaceutical manufacturing technologies

Summary of Discussions

Initial discussions were held with GE Healthcare in 2008. Initial contact was made by phone during which a high level overview of the potential for ^{14}C recycle was covered. A subsequent meeting was set up to develop this discussion further, however during the intervening period between the call and the meeting, arrangements had been made by GE Healthcare to sell of the radio pharmaceutical arm of the company. The result of this was that they were unable to contribute to the work undertaken under WP5 directly, although they did however maintain a record of the meeting which they passed on to the new owners of the radiopharmaceutical business, which was Quotient Bioresearch. A summary of the discussions with Quotient Bioresearch are covered under Section 2.3.

2.2 American Radiolabeled Chemicals (ARC Inc)

American Radiolabeled Chemicals, Inc. (ARC) is one of the leading suppliers of high quality radiolabeled and unlabeled chemicals in the world. They supply more than 4,000 radiolabeled (wide selection of ^{14}C and tritium labelled products) and unlabeled chemicals, which include:

- Amino Acids,
- Autoradiography Standards,
- Biological Chemicals,
- Carbohydrates,
- Ceramides,
- Coenzyme A's,
- Drugs,
- Fatty Acids,
- Glitazones,
- Inositides,
- Isoprenoids,
- Lipids,
- Neurochemicals,
- Nucleotides,
- PCBs,
- Peptides,
- Pesticides,
- Statins,
- Steroids,
- Toxins,

They have recently added two ^{14}C and two tritium standards for autoradiography that mimic the values previously offered by GE; they also offer a wide range of custom synthesis services using ^{14}C and tritium.

Summary of Discussions

Following the exit of GE Healthcare from the radiopharmaceutical market, attempts were made to identify other suppliers and/or users of ^{14}C internationally. A desk based research exercise was undertaken and a list of target companies identified. Each of these organisations was contacted and initial discussions held in which a high level overview of the aims of WP5's work on ^{14}C recycle was presented. Of the organisations contacted the majority of organisations either did not deal in the use or supply of ^{14}C, or otherwise used it in such small volumes that their existing supply routes were deemed adequate and therefore were not concerned with other sources of supply.

ARC Inc however did raise an interest in considering alternate supply route of ^{14}C, and suggested a meeting with the companies' president during November 2009, when he was visiting the UK. Unfortunately the meeting was postponed, several attempts were made to reschedule but to no avail. The feedback received from ARC Inc during telephone and email discussions was that they would only be interested in discussing the matter further if the recycle route could generate pure ^{14}C [1].

2.3 Quotient Bioresearch

Quotient Bioresearch is a leading provider of early stage and specialist drug development services to pharmaceutical, biotechnology and medical device clients worldwide.

Their range of capabilities covers the following areas:

- Radiochemistry
- Drug Discovery and Metabolism
- Agrochemical and Chemical Development
- Phase l/lla development
- Drug Product Optimisation
- ^{14}C Enabled Drug Development
- Biomarkers
- Bioanalysis
- Microbiology

They supply these capabilities either independently or integrated into tailored work programmes, such as:

- ^{14}C enabled Drug Development – delivered using their unique Clinic TM service
- Translational Pharmaceutics - enhances the speed, success and value from their pivotal phase I clinical studies.

Summary of Discussions

GE Healthcare sold its radiochemical business to Quotient Bioresearch, who in turn made contact with the WP5 leaders in June 2010. Initial discussions identified that Quotient Bioresearch as a major user of ^{14}C has an interest in identifying alternate supplies of the isotope. This is largely due to concerns over future security of supply as their primary source of ^{14}C has a limited lifespan.

A meeting was held on the 21st of July the between the WP5 leaders and representatives from Quotient Bioresearch. They key findings from this discussion were:

- Quotient has a unique position in the marketplace. It is the largest ^{14}C custom synthesis group and in addition to supplying ^{14}C labelled compounds direct to our customers is also a substantial user of ^{14}C labelled compounds in metabolism, clinical and environmental fate studies.
- This capability allows us to control the specification of ^{14}C labelled compounds used in house and we know that ^{14}C labelled compounds with specific activities of >20 mCi per mmole are perfectly fit for purpose in most applications.
- We are very interested in purchasing ^{14}C barium carbonate with a specific activity of >20 mCi per mmole for use in these 'in house studies'.

The specifications of ^{14}C carbonate which Quotient Bioresearch could utilise for synthesis are shown in Table 1 below [2]:

Table 1: Specifications of ^{14}C carbonate required by Quotient Bioresearch

Material	Specification	Comments
Barium [^{14}C] carbonate	ca.60 mCi per mmole ca.300 mCi per gram [ca. 96% ^{14}C]	This is the traditional 'full specific activity' material as supplied from nuclear irradiation.
Barium [^{14}C] carbonate	>20 mCi per mmole >100 mCi per gram [ca. 32% ^{14}C]	This is material at a specific activity which could be used in custom radiosynthesis to produce usable radiolabelled test compounds.

3 Conclusions

The key findings of this brief report for T.5.3.3 are that:

- The potential industrial recycle of ^{14}C over a number of years could use a significant proportion of the total i-graphite inventory, although it is most unlikely that most or all ^{14}C in irradiated graphite could be recycled. For example one UK manufacturer of products annually uses approximately 0.3% of the inventory of UK's Magnox reactors.
- Although ^{14}C is produced for manufacturers by reactor irradiation of nitrogen species and hence is available to them in high isotopic purity, the discussions revealed that a lower specific activity (i.e. isotopic dilution) would nevertheless be acceptable to manufacturers as input material for some applications. The possibility of recycling material directly from irradiated graphite (without isotope separation) was therefore examined. This would involve using "roasting" techniques to produce a fraction with the highest possible specific activity of ^{14}C from i-graphite, and selecting graphite with the highest possible ^{14}C activity for recycle. Unfortunately the gap is probably too large to bridge this way, since the specific activities required by the manufacturers are the order of 10^7 to 10^8 Bq/g compared with 10^5 Bq/g typical i-graphite inventory. Recycle of ^{14}C from graphite will therefore almost certainly require purification by isotope separation.
- The appropriate choice of graphite (and a "roasted" fraction from it) would allow any isotope separation process to be conducted on a small physical scale, thereby making the process more economic. More results will be required from "roasting" research to determine the maximum specific activity which can routinely achieved by this process, and this will ultimately determine the economics of recycle.
- There is no problem in producing from graphite fractions the chemical form of carbon needed for recycle [3]. Benzene is a key intermediate for production of products, but this can be produced from inorganic substances (e.g. the calcium carbide/acetylene route).

4 References

[1] Email dated: 25th September 2009 from Surendra Gupta, Ph.D. President of American Radiolabeled Chemicals, Inc

[2] Email dated 26th January 2011 from Grant Johnson, Director of Chemistry of Quotient Bioresearch.

[3] Carbowaste Report T-5.3.2 Report on Carbon Isotope Separation Methods. April 2011.

5 Glossary

ARC	American Radiolabeled Chemicals, Inc
GE	General Electric
PCB	Polychlorinated Biphenyls
WP5	Work Package 5