elements can be released, Horwitz describes this as a method for removing cations such as radium from f-block elements where the radium is considered a contaminant. The radium is washed through a column of DGA resin and disposed of leaving the purified and decontaminated actinide element to be stripped from the column.

The DGA resin described in Horwitz is only demonstrated to provide a separation efficiency of 10^2 for ^{223}Ra over ^{227}Ac (US 7553461, column 19 line 9). This is in the context of removing the radium and this it is not clear how applicable this would be to the preparation of radium rather than actinium, but even if this separation efficiency applied, it would fall well short of the at least 10^4 separation efficiency required to prepare pharmaceutical standard ^{223}Ra from a ^{227}Ac generator mixture. Thus, if the resin described in US 7553461 were used then this would apparently require two consecutive columns.

In view of the above, there is a considerable need for an improved method by which ^{223}Ra may be generated and purified for pharmaceutical use at a purity appropriate for direct injection into human subjects. It would be a considerable advantage if the method were to provide a high yield of ^{223}Ra, a low loss of ^{227}Ac or ^{227}Th parent isotopes and/or utilise only a small number of separation steps. It would be further advantageous if the method was rapid, was viable for relatively large (commercial scale) radioactive samples, included only a minimum number of manual handling steps, and/or was suitable for automation.

Brief Description ~~of the Invention~~

~~The present inventors have~~It has now been established that by optimising the conditions of use, and particularly by employing a combination of both forward and reverse flow, a highly effective separation of ^{223}Ra from an $^{227}Ac/^{227}Th$ generator mixture can be provided using only a single diglycolamide (DGA) extraction step. Furthermore, the generator mixture can be regenerated with an efficiency not previously reported. Recovery of both the ^{227}Th and ^{227}Ac allows for the potential long term, rapid-turnover, use of the system.

In a first aspect, the present invention therefore provides a method for the generation of ^{223}Ra of pharmaceutically tolerable purity comprising

i) preparing a generator mixture comprising ^{227}Ac, ^{227}Th and ^{223}Ra in a first aqueous solution comprising a first mineral acid;

ii) loading said generator mixture onto a DGA separation medium (e.g. resin);

iii) eluting said ^{223}Ra from said DGA separation medium using a second mineral acid in a second aqueous solution to give an eluted ^{223}Ra solution; and

iv) stripping the DGA separation medium of said ^{227}Ac and ^{227}Th by flowing a third mineral acid in a third aqueous solution through the DGA separation medium in a reversed direction (i.e. reverse flow);

The process will optionally and preferably also include the step of:

y) storing said mixture of ^{227}Ac and ^{227}Th for a period sufficient to allow ingrowth of ^{223}Ra by radioactive decay, whereby to re-form a generator mixture comprising ^{227}Ac, ^{227}Th and ^{223}Ra.

Further manipulation and/or preparation steps may be carried out on the eluted ^{223}Ra solution subsequent to step iii), however, the ^{223}Ra present in the eluted ^{223}Ra solution will preferably be of sufficient radiochemical purity for pharmaceutical use without further separation. Thus, in a preferred example~~aspect of the invention~~, ^{223}Ra of pharmaceutical purity is generated from a generator mixture comprising ^{227}Ac, ^{227}Th and ^{223}Ra in a single separation step. This is preferably possible on a commercial scale and using a method suitable for long-term application.

After ingrowth step y), the generator mixture may be re-used to generate a further batch of ^{223}Ra, and a single ^{227}Ac sample will preferably be used repeatedly (e.g. more than 10 times, such as 50 to 500 times). It is therefore preferable that the process be repeated from step i), or step ii) as appropriate.

In a further example~~aspect~~, the present disclosure~~invention~~ provides a solution or preparation of ^{223}Ra comprising less than 45 Bq ^{227}Ac per 1MBq ^{223}Ra. Such a solution or preparation is optionally formed or formable by any of the methods herein described, and is preferably formed or formable by the preferred methods herein described. Such solutions and/or preparations may be comprised in a pharmaceutical composition, such as one also comprising at least one pharmaceutically tolerable carrier and/or diluent.