block specific Silica Actinide Resin having P,P' di-octyl methane bisphosponic acid binding groups on a silica support. This provided relatively high purity, of less than $4x10^{-3}$% ^{227}Ac in comparison with ^{223}Ra, but required a large number of manual handling steps and was poorly suited for scaling-up or automation. Furthermore, because the resin irreversibly sorbed the mother and grandmother nuclei, the issue of radioactive damage to the resin becomes significant if such a resin is to be used for the commercial lifetime of an ^{227}Ac source (tens of years). This is especially the case on a commercial scale, where concentrations of isotopes need to be kept as high as possible to maximise batch sizes and minimise handling volumes.

No previously known method for the generation of ^{223}Ra addresses issues such as yield of ^{223}Ra, speed of the purification process, automation, minimising of wasted isotopes and corresponding production or radioactive waste or any similar issues associated with commercial-scale production. Furthermore, all methods known to produce ^{223}Ra of viable pharmaceutical purity use specialist resins which cannot be guaranteed to be available and are potentially more difficult to validate as reliable. Guseva *et al.* (Radiochemistry **46**, 58-62 (2004)) proposed a basic generator system for ^{223}Ra using an anion exchange method developed for extracting radium from environmental samples. This, however, was on a very small scale and never intended or indicated as providing material of pharmaceutical purity.

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 and/or ^{227}Th parent isotopes and/or utilise widely available separation media. 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 now established that by separation of a $^{227}Ac/^{227}Th/^{223}Ra$ generator using a strong base anion exchange resin, followed by separation utilising a strong acid cation exchange resin, a ^{223}Ra solution of very high radiochemical purity may be produced while providing a number of desirable advantages in the method.

In one aspect, there is provided 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;

ii) loading said generator mixture onto a strong base anion exchange resin;

iii) eluting said ^{223}Ra from said strong base anion exchange resin using a first mineral acid in an alcoholic aqueous solution to give a first eluted ^{223}Ra solution;

iv) loading the ^{223}Ra of the first eluted ^{223}Ra solution onto a strong acid cation exchange resin; and

v) eluting the ^{223}Ra from said strong acid cation exchange resin using a second mineral acid in aqueous solution to provide a second eluted solution.

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

i) forming a generator mixture comprising ^{227}Ac, ^{227}Th and ^{223}Ra;

ii) loading said generator mixture onto a strong base anion exchange resin;

iii) eluting said ^{223}Ra from said strong base anion exchange resin using a first mineral acid in an alcoholic aqueous solution to give a first eluted ^{223}Ra solution;

iv) loading the ^{223}Ra of the first eluted ^{223}Ra solution onto a strong acid cation exchange resin; and

v) eluting the ^{223}Ra from said strong acid cation exchange resin using a second mineral acid in aqueous solution to provide a second eluted solution.

The process will optionally and preferably also include either one or both of the steps of:

x) eluting said ^{227}Ac and ^{227}Th from said strong base anion exchange resin using a third mineral acid in aqueous solution, whereby to recover a mixture of ^{227}Ac and ^{227}Th; and

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.

Step x) may be carried out at any point following step iii) of the above-described process. Step y) will begin immediately following elution step iii) and may occur primarily on the anion resin (i.e. before or without step x)) and/or after recovery of the ^{227}Ac and ^{227}Th mixture from the resin (i.e. after step x)).

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). If the ^{227}Ac and ^{227}Th mixture is not eluted from the strong base anion exchange resin then the process may be repeated from step iii). Preferably, however, step x) will be carried out and the ^{227}Ac and ^{227}Th mixture eluted from the strong base anion exchange resin. In this case the process will be repeated from step i) or step ii).

In a further exampleaspect, the present disclosureinvention provides a solution of ^{223}Ra comprising less than 45 Bq ^{227}Ac per 1MBq ^{223}Ra, preferably a solution of ^{223}Ra comprising less than 10 Bq ^{227}Ac per 1MBq