

The application

- 5 The application relates to a process for increasing the efficiency of extraction of 6-acetyl-4,1',6' trichlorogalactosucrose (6-acetyl-TGS) and 4,1',6' trichlorogalactosucrose (TGS also known as sucralose) from aqueous solution by addition of salt. The invention helps in reducing the quantity of solvent needed for achieving substantial extraction of 6-acetyl TGS or TGS and leads also to extraction of TGS which is substantially free from polar impurities.
- 6 Sucralose is a sweetener with a sweetness intensity several hundred times that of sucrose and is derived from sucrose by replacing the hydroxyl groups in the 4, 1' and 6' positions with chlorine.
- 7 For many years, researchers have been striving to commercially manufacture sucralose, and synthesising it has proven to be technically challenging. Research has since moved on to purifying and isolating sucralose from reaction mixtures.
- 8 The inventors have found that (i) TGS in aqueous solution could be selectively extracted into organic solvents which are water immiscible or nearly immiscible solvents in relatively lesser quantity of solvent if the aqueous solution containing TGS is saturated with salts (including sodium chloride) ie. a reduction in the amount of solvent consumption (when compared to extraction without salt saturation) and (ii) the organic solvent extract obtained after extraction of salt saturated aqueous solution of TGS contained very little of the polar impurities (ie. polar impurities following extraction of the aqueous TGS solution with solvent results in the polar impurities being left behind in aqueous phase -with the current invention viewed as a method for removal of polar impurities from the crude TGS).

The claims

- 9 The latest set of claims on file were those filed on 22 February 2010 and this is the set upon which I will base my decision. There are 5 claims in total, with claim 1 being the only independent claim and reading:

Claim 1:

1. A process of extraction of 6-acetyl-4,1',6' trichlorogalactosucrose (6-acetyl-TGS) and/or 4,1',6' trichlorogalactosucrose (TGS), from aqueous solution, containing or not containing other solutes or suspended particles, into an organic solvent which is water immiscible or sparingly water miscible, wherein:

(a) the said aqueous solution is substantially free from organic solvents including a tertiary amide including dimethylformamide,

(b) one or more salts selected from sodium chloride, sodium acetate, calcium chloride, barium chloride, potassium chloride or potassium acetate are added to the aqueous solution prior to the extraction by organic solvent,

whereby the concentration of added salt or salts is/are sufficient to increase the extraction of 6-acetyl-TGS or TGS into the extracting solvent, and optionally, sufficient to effect selective extraction of 6-acetyl-TGS or TGS substantially free from polar impurities.

Issue to be decided

- 10 The issue I now have to decide, based on the papers available to me, is whether the claims satisfy section 1(1)(b) of the Patents Act 1977 (the "Act"), i.e. whether they comprise an inventive step.

The Law

- 11 The law regarding inventive step is found in sections 1 and 3 of the Act. The relevant parts read as follows:

Patentable Inventions

1.-(1) A patent may be granted only for an invention in respect of which the following conditions are satisfied, that is to say –

- (a) ...
- (b) it involves an inventive step;
- (c) ...

and references in this Act to a patentable invention shall be construed accordingly.

- 12 Section 3 defines what is meant by 'inventive step'.

Inventive Step

3. An invention shall be taken to involve an inventive step if it is not obvious to a person skilled in the art, having regard to any matter which forms part of the state of the art by virtue only of section 2(2) above (and disregarding section 2(3) above).

- 13 I do not propose to quote sections 2(2) and 2(3) here, but it follows from these that the state of the art comprises all matter which has at any time before the priority date of the application been made available to the public, whether in the UK or elsewhere.

14 The correct test for determining inventive step is the structured approach found in *Windsurfing International Inc. v Tabur Marine (Great Britain) Ltd*, [1985] RPC 59 as reformulated by Jacob LJ in *Pozzoli SPA v BDMO SA* [2007] EWCA Civ 588 (see paragraph 23 of the Court of Appeal's judgment). The four steps of the test are now:

(1)(a) Identify the notional "person skilled in the art"

(1)(b) Identify the relevant common general knowledge of that person;

(2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;

(3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;

(4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

Applying the Windsurfing/Pozzoli test

Step 1(a): Identify the notional "person skilled in the art"

15 From the papers before me, there appears to have been no problems between the applicant and examiner in identifying the notional "person skilled in the art". The applicant has identified the technical field of the present invention as lying in that of preparative chemistry for the purpose of obtaining substantially pure sucralose, identifying the notional "person skilled in the art" as being a synthetic organic chemist knowledgeable in the field of sugar synthesis, especially of chlorinated sucralose. The examiner has made a similar identification. I am satisfied that both applicant and examiner have given a good identification of the notional "person skilled in the art".

Step 1(b): Identify the relevant common general knowledge of that person

16 The applicant asserts that the notional skilled person would have knowledge of accepted methods of synthesis and purification of sucralose at the priority date of the present invention ie. 10 December 2004.

17 The examiner similarly asserts that the notional skilled person would be aware of general organic synthetic methods, especially of known synthetic schemes used for TGS synthesis, but has spelt out in more detail what knowledge he would expect the skilled person to have. The skilled person would be aware of the general physical properties of sugar derivatives, such as their solubility in organic and aqueous phases, and recognise also that most sugar derivatives, due to their abundance in hydroxyl groups, are very soluble in water. The skilled person would be aware of general purification methods of sugar derivatives such as chromatography, distillation and extraction and also of general preparative methods including methods to increase the yields of such purification methods. In particular, the examiner asserts that the skilled person would be aware of the technique of "salting-out", commonly used in extraction processes, where the addition of salt (eg. sodium chloride) to an aqueous phase increases the polarity of this phase which has the effect of increasing the solubility of very polar organic compounds whilst less polar organic compounds are less soluble.

18 To support this assertion, the examiner has pointed to AULT (Techniques and Experiments for Organic Chemistry, Fifth Edition, 1994, pages 110 - 112, especially 112), a typical standard chemistry text book used to support undergraduate teaching and to the section relating to "salting-out" used in the field of liquid extraction. The paragraph bridging pages 111 and 112 reads:

"If the distribution coefficient for a substance to be extracted from water is much less than 1 - that is, if the ratio at equilibrium of the concentration in the organic solvent to the concentration in water is much less than 1 - a simple extraction process will not give a satisfactory recovery. The distribution coefficient can sometimes be increased by adding sodium chloride or sodium sulphate to the aqueous solution, since the solubility of most organic compounds is less in salt solutions than in water (The interpretation for this phenomenon, known as salting out, is given in section 22.1.) Alternatively, the distribution coefficient can be increased by using an organic solvent that is a better solvent for the type of compound being extracted. For substances with oxygen-containing functional groups, ethyl acetate and n-butyl alcohol are probably better solvents than non-oxygen-containing solvents."

19 Since both applicant and examiner have identified that the notional "person skilled in the art" would be familiar with methods for purifying sucralose, in particular liquid extraction, I believe it wholly reasonable to expect that skilled person to be familiar with techniques routinely used in conjunction with liquid extraction, such as "salting-out".

20 Having carefully read through the applicant's arguments, the applicant does not appear to contest that "salting-out" would not form part of the common general knowledge of the notional person skilled in the art. However, the applicant has clearly argued that "salting-out" is not an obvious step to make in conjunction with the prior art to arrive at the present invention and I will clearly need to take this into account when considering step 4.

Step 2: Identify the inventive concept of the claim in question or if that cannot readily be done, construe it:

- 21 The applicant has identified the inventive concept of claim 1 as being concerned with obtaining substantially pure TGS (sucralose) or 6-acetyl-TGS by a method of liquid extraction from an aqueous solvent into an organic solvent, without requiring the use of an excessively large amount of organic solvent, which is achieved by adding one or more salts selected from sodium chloride, sodium acetate, calcium chloride, barium chloride, potassium chloride or potassium acetate into the aqueous solution prior to the extraction by organic solvent, which promotes migration of TGS or 6-acetyl-TGS into the organic extraction phase.
- 22 The examiner has similarly construed the claimed inventive concept as a process of extraction of 6-acetyl-TGS or TGS from an aqueous solution into an organic solvent, wherein (a) the aqueous solution is substantially free from organic solvents (such as DMF) and (b) sufficient amounts of one or more salt/s are added to the aqueous solution prior to the extraction by an organic solvent. The examiner asserts that this has the effect that the amount of product which is transferred from the aqueous phase to the organic phase is increased (or that less extraction solvent has to be used to reach the same yield) and the effect that more polar impurities remain in the aqueous phase (report dated 14/09/09, para 9).
- 23 In my view, the inventive concept is clearly discernable from claim 1 and this is in full agreement with both the applicant and the examiner's interpretation.
- 24 Given that there have been several rounds of argument/amendment of the claims, I note that the inventive concept of claim 1 has fundamentally remained unchanged.

Step 3: Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed

- 25 The examiner cited two documents, US 4380476 (MUFTI) and WO 03/076453 A1 (McNEIL) as forming part of the state of the art and has asserted that the difference between each of these documents and the inventive concept is the lack of adding salt to the aqueous solution prior to the extraction by organic solvent (ie. step (b) of current claim 1).
- 26 The examiner has asserted that this difference in itself amounts to "salting-out", (already discussed in detail in paragraphs 17 and 18) and that this technique is no more than a routine technique used in conjunction with solvent extraction when seeking to purify/increase yield of a desired compound and would form part of the common general knowledge of any chemist/research chemist including the notional "person skilled in the art".

- 27 The applicant has disputed the relevance of MUFTI in assessing the inventive step of the current application (see below) but they have agreed that McNEIL exemplifies the state of the art known by the skilled person in the relevant technical field of the present invention, against which the inventive step of the present invention should be assessed. Likewise, the applicant has identified the difference between the inventive concept of claim 1 and McNEIL as being the lack of use of salts added to the aqueous solution prior to the extraction by organic solvent, which of course, is step (b) of current claim 1.
- 28 Both applicant and examiner have therefore identified the same difference between McNEIL and the inventive concept ie. the lack of a step corresponding to step (b) of claim 1 (the “salting-out” step) and from my reading and understanding of the respective arguments, I am fully satisfied that this is indeed the case.
- 29 From reading MUFTI and taking into consideration the examiner’s arguments, I too can see that the difference between what is disclosed in Example 5 of this document and the inventive concept is exactly the same as what has already been identified by the examiner and the applicant in respect of McNEIL ie a lack of a step (b) as defined in current claim 1. However, given that the applicant has disputed whether MUFTI does indeed form part of the state of the art, I will now give this issue further consideration.

Does MUFTI form part of the state of the art?

- 30 The applicant has asserted that MUFTI is not relevant prior art to the present invention because it does not concern the same technical problem as the present invention, namely in providing two non-obvious developments of (a) a more efficient extraction step and (b) improved removal of polar impurities. The applicant has observed that MUFTI is concerned with addressing the problem of the selective protection of sucrose prior to chlorination and has pointed out that no mention has been made of any problems associated with the purification of TGS once protected, chlorinated and de-protected, submitting also that this document does not disclose teaching relevant to reach the present invention.
- 31 From careful reading of MUFTI, it teaches primarily in my view, a process for preparing sucralose. It recognises that the process is generally made difficult by chlorination issues but nevertheless has identified a route that with “careful monoacylation of sucrose will give a mixture of sucrose monoacylatesand that, if the mixed acylated derivative is chlorinated, it is possible to separate the required TGS from the other products produced, without undue difficulty.” (column 1 lines 60-68 - my emphasis).

- 32 Whilst this document is also concerned with separating the TGS from the crude reaction products, it does not appear to me to be seeking to optimise the yield of the TGS so produced. Indeed, it states in column 1 lines 45-47 that “there is a need for a process which will give the desired sweetener in a reasonable yield from sucrose in a small number of stages.” (again-my emphasis)
- 33 It is acknowledged also in column 5 lines 56-61 that “... the success of the overall process will depend in part on the fact that TGS itself can be isolated without undue difficulty from the deacetylated mixture of chlorinated sucrose derivatives obtained”, through invoking the use of standard routine laboratory practices/ techniques to obtain the TGS - be it via chromatography or liquid-liquid extraction - in a yield which is considered to be reasonable.
- 34 I take from this that the researchers in MUFTI would not in this instance be looking towards improving the yield of TGS recovered, instead being satisfied that TGS has indeed been produced with a good level of purity (99%) and satisfied with a reasonable yield (about 5%).
- 35 How then, would knowledge of this document in combination with “salting-out” get you to the present invention? In my view it does not without invoking the benefit of hindsight. Since the researchers in MUFTI routinely use solvent extraction techniques, I believe it would be wholly reasonable to expect them to be familiar with the technique of “salting-out” and to adopt it during the extraction step if they so desired, to seek to improve the TGS yield - the line of argument which the examiner has taken in the report of 14/01/09. But there is no motivation in MUFTI to do so.
- 36 I therefore accept the applicant’s arguments in respect of MUFTI and agree that it does not form part of the state of the art for assessing obviousness of the present invention.

Starting point for assessing obviousness

- 37 Both applicant and examiner have indicated that McNEIL is the starting point for assessing obviousness of the present invention. The examiner has indicated that the starting point for assessing obviousness is indeed the second extraction step in McNEIL, which I fully accept.

Step 4: Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

- 38 The applicant has argued throughout that the difference is not an obvious step for the notional “person skilled in the art” to have made whilst the examiner has maintained throughout that the difference is a step which would be obvious to the skilled person applying their common general knowledge, thus rendering the invention as currently worded in claim 1 non-inventive.

- 39 Having identified the difference that exists between the cited prior art and the invention as claimed, it is now for me to decide whether said difference would have been obvious to the notional “person skilled in the art” at the priority date of the invention or whether a certain degree of invention was required on the skilled person’s part.
- 40 In doing so, I must avoid looking at the cited prior art under the influence of the present application and should attempt to place myself in the position of the skilled person faced with the problem at hand. I must therefore be aware of using hindsight or *ex-post facto* analysis to arrive at the invention.
- 41 Accepting McNEIL as the starting point for assessing obviousness and having found that the only difference between the invention as claimed and that disclosed in McNEIL is the apparent lack of adding salt to the aqueous solution prior to the extraction by organic solvent (ie. step (b) of current claim 1), I must decide whether this difference would have been obvious to the notional “person skilled in the art”.
- 42 From the papers, it is clear to me that the examiner and applicant have been engaged in extensive arguments on why/why not the invention is “obvious to try”, with the applicant drawing also on “new advantages” and “why hasn’t it been done before?” to argue their case.
- 43 The examiner has argued that the invention as currently worded would be obvious to the skilled person seeking to improve the yield of the second extraction process disclosed in McNEIL. From this document, the examiner has observed that (a) polar impurities have been left behind in a salty aqueous phase and (b) the majority of the TGS has already been extracted to the organic phase. Consequently, an expert seeking to increase the yield of the extraction process will know that TGS is very soluble in water and would therefore realise that the yield of the extraction process could be improved by invoking generally known techniques for improving extraction processes of water soluble products. The expert would therefore, with a reasonable expectation of success, turn to the “salting-out” technique: a simple experiment would tell him whether his expectations of success were justified. The examiner has therefore argued that the invention as claimed does not involve an inventive step over the disclosure in McNEIL when combined with the common general knowledge of “salting-out”.
- 44 The applicant argues that the difference constitutes an inventive step because the state of the art, as exemplified by McNEIL, would not motivate a skilled person to modify known methods of extractive purification of sucralose to use salts added to the aqueous solution prior to the extraction by organic solvent and thus argue that from McNEIL, a skilled person would not only need to ignore an essential extraction step in the process described in that document (a two extraction step process) but would also need to consider adding salt to the aqueous solution, as per the current invention.

- 45 Whilst the applicant has acknowledged that although certain techniques of adding salts to increase the polarity of an aqueous phase may be known methods of organic chemistry in general (amongst a plethora of other possible techniques) as discussed in AULT, they have stressed that a skilled person could use such a technique, but that there is no suggestion or motivation in the prior art that would motivate a skilled person such that he would use this technique with a reasonable expectation of success in the purification of TGS (sucralose) or 6-acetyl-TGS. They have argued that it is not obvious to combine the teachings of McNEIL with the common general knowledge to arrive at the current invention.
- 46 Having given careful thought to both sets of arguments, I do not accept the applicant's argument that a skilled person with knowledge of McNEIL and wanting to improve further the method of extracting TGS from aqueous solution to organic solvent where the TGS is free from polar impurities would not be motivated to at least undertake a routine experiment to determine whether there was anything to be gained by "salting-out" (ie. adding salts to the aqueous solution containing TGS & impurities prior to the second extraction with organic solvent). I therefore accept the examiner's arguments, my reasoning being as follows:
- 47 Considering the issue afresh, McNEIL teaches extractive methods for purifying sucralose and through their specific 2-step extraction process, have identified that the TGS obtained is of better purity (in particular, free of polar impurities) and, in obtaining the purified TGS, they have avoided using large volumes of solvent through less repetitive extractions of TGS required in their process. Accepting that the starting point for assessing obviousness is indeed the second extraction step because this is the point at which the TGS is extracted into organic solvent (ethyl acetate in this case), I believe that researchers building on McNEIL will, at this point, consider how they can go about further increasing the purity of TGS and extract more of the TGS into the organic solvent (to give a better yield of TGS). They will already know from McNEIL that that method has been successful in reducing polar impurities in the final TGS product.
- 48 I believe researchers at this stage would be minded to experiment with the standard laboratory technique of "salting-out", with an expectation that the effect of adding salts to the aqueous solution containing TGS and polar impurities prior to extraction with organic solvent would, as a matter of course, lead to the transfer TGS into the solvent (ethyl acetate) phase, leaving the more polar impurities as well as the inorganic salts behind in the aqueous phase. A simple experiment would indicate the likelihood of success in this scenario.
- 49 In my view therefore, the invention as currently worded in claim 1 clearly lacks inventiveness because the difference identified in step 3, namely the addition of salts to the aqueous solution containing TGS prior to extraction with organic solvent with there being a likelihood of success, is nothing more than a routine step, requiring no inventive ingenuity on behalf of the skilled person ie. the present invention as currently worded does not make available to the skilled person, something that he would not reach by normal exercise of his skill.

Advantages of the invention and why hasn't it been done before?

- 50 The applicant has argued that the current invention is not obvious because it has identified significant advantages over the prior art, namely a more efficient method for extraction of TGS from aqueous solvent to organic solvent using less solvent and improved removal of polar impurities. The examiner has argued, correctly in my view, that McNEIL has already identified such issues and so this line of argument does not persuade me that the advantages identified by the applicant render the invention non-obvious. The examiner has brought the focus of the argument back to the actual construction of claim 1 which covers the use of the stated salts in any extraction of TGS or 6-acetyl-TGS where other organic solvents are essentially absent, which is a conventional liquid-liquid extraction.
- 51 The applicant has also argued that the invention is not obvious because it hasn't been done before, pointing out that commercial production of sucralose has occurred since the publication of MUFTI (April 1983) and that in the patent literature since then and up to 2005, none of the processes for sucralose production has implemented the use of salt for extraction of sucralose from aqueous solutions in organic solvents despite the substantial benefits demonstrated by the present invention.
- 52 I have given careful consideration to this line of argument from the applicant and again, I am not persuaded that this confers inventiveness on the current invention. This does not detract from the fact that, in my view, the applicant has simply invoked the use of a standard "salting-out" technique in liquid extraction in order to isolate, purify and improve the yield of the TGS extraction.
- 53 In my view, the current invention hasn't been done before because prior to McNEIL, (see page 1 lines 18-20 of this document which reads: "...*the isolation of sucralose in highly purified from this complex mixture of contaminants heretofore has received relatively little attention.*"), the focus has been on synthesising sucralose with crude isolation of the TGS product and not on methods of further purifying TGS from the reaction mixture, using less solvent in the extraction process or seeking to increase the yield.
- 54 Having devised methods for synthesising sucralose, it's my view that researchers like McNEIL have now started to focus on ways of improving the purity of the sucralose obtained (so as to improve its taste etc) and the extraction yield and that starting from the 2nd extraction step highlighted by the examiner in McNEIL, the adopting the routine technique of "salting-out" ie. adding salt to an aqueous solution containing TGS/impurities prior to extraction with organic solvent, is an obvious development of the teachings of this document.
- 55 Having given thorough consideration to the arguments, I can see nothing in the applicant's line of argument which persuades me that the invention as currently worded in claim 1 is not obvious in the light of the prior art and the common general knowledge.

- 56 I note the applicant has referred to US 20090299054 (TATE & LYLE) (which does not form part of the state of the art since its priority and publication date is after the priority date of the present invention) which they claim supports the inventiveness of the present invention, by providing evidence of further development in the technical field after publication of the present application. However, It is interesting to note that claim 1 of (TATE) is very specific, requiring the extraction process of an aqueous solution containing TGS or 6-acetyl TGS, other chlorinated sugars, dimethylammonium chloride and a further chloride from into organic solvent is dependent on increasing the ratio of further chloride and dimethylammonium chloride in the aqueous solution prior to or during extraction into organic solvent, compared with claim 1 of the present invention which by comparison is very broad. In my view, (TATE) does not support the applicant's argument that the current invention is non-obvious and if anything, strengthens the argument that the monopoly sought by the current claim 1 is too broad.
- 57 To summarise, on the basis of the arguments and documentation available to me, I find the invention as currently worded in claim 1 to be lacking an inventive step on the basis of McNEIL when combined with the common general knowledge.
- 58 Regarding appendant claims 2-5, I am of the view that the features disclosed would be common in the field of solvent extraction and would not confer inventiveness on claim 1 if incorporated therein. I note that the organic solvents defined in claims 4 and 5 are typical solvents for use in solvent extraction for extracting sucralose and related derivatives and are disclosed in both MUFTI and McNEIL (page 10 line 22 to page 26 line 2).

Conclusion

- 59 I find that claims 1-5 do not comply with section 1(1)(b) of the Act insofar as they do not involve an inventive step.
- 60 However, I note the examiner has indicated that the inventive step objection could possibly be overcome by suitable amendment to claim 1.
- 61 As things stand, I note the compliance period (as extended) ended on 14th May 2010. However, it is possible for the applicant to request a further extension to the compliance period and, if that extension is allowed, that would move the compliance date to beyond the date of this decision and it would then fall within the 28 day appeal period. Section 20(2) would then apply. Following section 20(2)(a), if the decision is appealed, the compliance period would then be set by the court and following section 20(2)(b) if the decision is not appealed, the compliance date would be the 28th day of the appeal period i.e. 6th August 2010.
- 62 Therefore I order as follows:

- 63 If the compliance date remains 14th May 2010, the application will be treated as refused under section 20(1), since I have found that it did not comply with the Act and Rules on that date
- 64 If the applicant makes a successful request to further extend the compliance period, the application will then be remitted to the examiner in order to allow the applicant an opportunity to file amendments to overcome the outstanding objection.

Appeal

- 65 Under the Practice Direction to Part 52 of the Civil Procedure Rules, any appeal must be lodged within 28 days.

C L Davies

Deputy Director acting for the Comptroller