Mr K Casarin
Copy of Appeal Decision
– Your Brief

TGA THERAPEUTIC GOODS ADMINISTRATION
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Commonwealth Department of Health and Ageing

FAXED 22/02/02

[redacted]

Dear [redacted]

Thank you for your letter of 17 December 2001 seeking review of the decision ("initial decision") made on 18 September 2001 by Ms Allison Rosevear, as Delegate of the Secretary, to cancel the listing on the Australian Register of Therapeutic Goods of the product [redacted]

I am the Minister's Delegate for the purposes of the review.

Result of my reconsideration of the initial decision.

I have decided to confirm the initial decision.

Findings of fact

My findings on material questions of fact and the evidence on which these findings are based are given below.

(1) The Therapeutic Goods Administration (TGA)notified the sponsor and the sponsor's then agent on 12 July 2001 of a decision to list as a therapeutic good on the Australian Register of Therapeutic Goods [redacted]. Evidence- copy of certificate and other documentation on file.

(2) On 2 August 2001, by means of a notice under section 31 of the Therapeutic Goods Act 1989, the sponsor was requested by the TGA for the purposes of finalising the listing to provide additional information concerning the manufacturing procedure for the active ingredient and the method for analysis of the standardising components together with the validation data for the method. Evidence- copy of notice on file.

(3) On 18 September 2001 the Delegate of the Secretary having reviewed the information submitted in response to (2) and having received the expert advice of the Therapeutic Goods Administration Laboratories conveyed to the sponsor by Notice under section 30(1)(e) of the Therapeutic Goods Act 1989 the initial decision to cancel the listing of the product. The basis for the decision was ,in brief, that the review of the submitted information indicated that the

active ingredient did not meet the definition of a herbal substance as set out in the Schedules to the Therapeutic Goods Regulations because the manufacturing process included steps that constituted purification and that such steps are not permitted by the definition of herbal substance. Evidence- copy of Notice and associated documentation on file.

My consideration of your appeal

I shall address the four points in your appeal document seriatim:

Point 1 – the material is accepted as a herbal extract throughout the world.

I have noted this point but do not accept it as a ground for changing the decision. To be eligible for listing in Australia a herbal substance must meet the definition in the Regulations. I note that you in effect concede this in the narrative about this Point.

Point 2 – the manufacturing process does not produce a purified substance but merely concentrates the soy.

I have examined material submitted previously as well as Attachment 1 to your letter seeking the review. I have examined the [redacted] patent document which was described by [redacted] as including a very extensive description of the process and process conditions.

The Process is described as being for "the production of isoflavone fractions from soy". The abstract of the patent indicates that the process is used "to initially separate the (isoflavone)fractions"; that the process then "further selects desired isoflavone molecules by size"; and that "the resulting permeate is put through a resin adsorption process carried out in at least one liquid chromatography column to further separate the desired isoflavone fractions." I do not accept that such a process "merely concentrates the soy."

I find my view supported by the advice of the TGA Laboratories which found that substances of interest (isoflavone fractions) are adsorbed onto a resin which is then subjected to washing and elution with an aqueous ethanol gradient such that fractions containing isoflavones are then concentrated. I accept the view of the TGA Laboratories that this process constitutes a purification step of the sort that might occur in the manufacture of a drug substance.

It is clear also that the relative proportions of individual isoflavones in the final product of the process may be varied by making changes in the process parameters. The patent document states (page 12 of 16) "The breakdown of the *isoflavones* that were recovered are set forth in Table III. The conclusion is that each of the tests shows results that are attractive for certain uses. Therefore, the practitioner (in this context ,the processor of the soy) will select the particular process which best reflects the results that he seeks."

I think that if the manufacturing process did in fact merely concentrate the soy, the relative proportions of the individual isoflavones should remain approximately the same.
I note however that the percentage concentrations of isoflavones expressed as a proportion vary greatly between [redacted] and [redacted] in Attachment 1. For example, there is a factor of 1028.9 between the two for Daidzin but a factor of 0.99 between the two for Malonyl Daidzin. I do not accept that this is consistent with mere concentration of the soy.

Point 3 – that the manufacturing process should be called extraction and that the process meets the TGA definition.

The letter at Attachment 2 misquotes Perry's handbook when it claims "Adsorbents are natural or synthetic materials of amorphous or crystalline structure." The reference is in fact to "Sorbents" " and not "adsorbents."

The quote does not say that sorption is "considered to include gas absorption and liquid extraction." What is actually stated is that "Sorption ***could be*** (my emphasis) considered to include gas absorption and liquid extraction."

I have noted that the same reference ,under Adsorption , states that major uses of liquid-phase adsorption include "2. Recovery of biological chemicals (antibiotics,vitamins,flavourings) from fermentation broths or plant extracts." It is clear to me that absorption can be used as part of a process for separation , purification and concentration of individual constituents of a conventional plant extract. That is something more than what is conventionally understood by extraction.

Point 4 – that specific fractions are not selected.

You claim that Dr Cumming was in error in stating ".....and the fractions containing isoflavones are then concentrated. In other words, specific fractions are selected."

I do not accept this. I think that Dr Cumming's statement is accurate . Isoflavones are concentrated in the process. I do not think this is central to the issue. What is central is that the process not only concentrates isoflavones but also changes their concentrations and thus relative proportions and ,further, that those concentrations and relative proportions can be varied by varying process parameters.

Reasons for my decision

The definition of herbal substance in Regulation 2 of the Therapeutic Goods Regulations requires that the substance is obtained only by drying, crushing, distilling, extraction, expressing, comminuting, mixing with water, ethanol, glycerol or aqueous ethanol and is not subjected to any other treatment or process other than a treatment or process that is necessary for its presentation in a pharmaceutical form. As set out in my comments on the various Points above, I am of the opinion that the Novasoy process involves more than extraction as it is conventionally understood and not merely a process to concentrate the isoflavones in an extract suitable for tabletting and encapsulating. In my view, it is a process which permits considerable manipulation of the content of individual isoflavones in the final product and is thus a process outside those permitted by the definition.

The Administrative Appeals Tribunal

Except where subsection 28 (4) of the Administrative Appeals Tribunal Act 1975 applies, you may apply for a statement setting out the reasons for my decision. Subject to that Act, you may make application to the Administrative Appeals tribunal for review of my decision.

In view of the statement of reasons set out above, I believe that subsection 28 (4) of the Administrative Appeals Tribunal Act 1975 applies.

Yours sincerely

John McEwen
Delegate of the Minister for Health and Ageing
21 February 2002.