Federal Court  Cour fédérale

Date: 20200407

Docket: T-1603-18

Citation: 2020 FC 397

Ottawa, Ontario, April 7, 2020

PRESENT: The Honourable Mr. Justice Barnes

BETWEEN:

GLAXOSMITHKLINE BIOLOGICALS S.A.

Applicant

and

THE MINISTER OF HEALTH

Respondent

PUBLIC JUDGMENT AND REASONS

(Identical to the Confidential Judgment and Reasons issued on March 20, 2020)

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[1] This application by GlaxoSmithKline Biologicals S.A. [GSK] challenges a decision by Health Canada dated August 3, 2018 refusing to issue a Certificate of Supplementary Protection [CSP] in respect of Canadian Patent No. 2,600,905 [the 905 Patent] and the drug SHINGRIX®.

I. The 905 Patent

[2] GSK is the owner of the 905 Patent. The 905 Patent pertains to a novel and improved vaccine useful in the prevention or amelioration of shingles in adults older than 50, or in immunocompromised persons. The invention is said to relate to compositions capable of inducing an immune response against the Varicella Zoster Virus including the combination of an antigen and an adjuvant. Claim 4 describes such a combination in the following way:

> 4. An immunogenic composition or vaccine comprising a Varicella Zoster Virus (VZV) gE antigen truncated to remove the carboxy terminal anchor region and consisting of the amino acide sequence of SEQ ID NO:1, in combination with an adjuvant comprising QS21, 3D MPL and liposomes comprising cholesterol.

[3] Claim 1 is a claim to the use of such a composition to prevent or ameliorate shingles.

[4] The 905 Patent was filed on March 1, 2006 and issued on May 5, 2015. It will expire on March 1, 2026.

II. The Decision Under Review

[5] The decision refusing a CSP to GSK is contained in an August 3, 2018 letter from the Director General of Health Canada's Therapeutic Products Directorate [the Minister]. Set out below are the key parts of the decision:

> **2. Medicinal ingredient or combination of medicinal ingredients?**
>
> The single medicinal ingredient approved in SHINGRIX is Varicella Zoster Vials (VZV) g1ycoprotein E (gE).
>
> The Notice of Compliance (NOC) for Submission No. 200244 dated October 13, 2017 lists "Varicella Zoster Virus (VZV) glycoprotein E (gE)" as the single medicinal ingredient for the drug SHINGRIX.
>
> The submission application form (HC-SC 3011) for Submission No. 200244 lists under item 56 gE antigen as the single medicinal ingredient.
>
> The Product Monograph ("PM") for SHINGRIX on page 3 in the table labeled "Summary Product Information" lists "Varicella Zoster Virus (VZV) glycoprotein E (gE)" as the single medicinal ingredient under the heading "Dosage Form / Strength per 0.5 mL dose." In contrast, cholesterol, dioleoyl phosphatidylcholine (a component of the liposomes as noted on page 14 of the PM), *Quillaja saponaria* Molina, fraction 21 (QS21), and 3-O-desacyl-4'-monophosphoryl lipid A (MPL) are all listed as non-medicinal ingredients in the same table. The Summary Product information is in Part I: Health Professional Information.
>
> In your representations on page 1, you submit that the "OPML has incorrectly classified the adjuvant in the 905 Patent and contained in SHINGRIX® as a non-medicinal ingredient."
>
> The TPD disagrees. The TPD has consulted with the Biologics and Genetic Therapies Directorate ("BGTD") and has confirmed that Health Canada's position is that adjuvants are not medicinal ingredients, and specifically that adjuvant $AS0_B$ is not considered a medicinal ingredient in SHINGRIX.

The Health Canada Guidance Document "Harmonized Requirements for the Licensing of Vaccines and Guidelines for the Preparation of an Application" ["Vaccine Guidance Document"] considers adjuvants to be excipients, and not medicinal ingredients. On page 24 under the description of Section 3.2.P.4.6 Novel Excipients (name, dosage form), the Vaccine Guidance Document states "[f]or any novel excipient, including adjuvants, preservatives and stabilizers..." (emphasis added). This phrase is repeated on page 27 under the description of Section 3.2.A.3 Excipients. Further, Dr. Brian Barber, in his affidavit that you provided with your representations, acknowledges that the Vaccine Guidance Document "does not include adjuvants as part of the 'drug substance,' but as part of the 'drug product.'"

The identification of VSV gE as the single medicinal ingredient in SHINGRIX on the NOC, the submission application form for SHINGRIX, and on page 3 of the PM is consistent with the position of Health Canada as set out in the Vaccine Guidance Document.

…

In your representations, you also refer to an email from Health Canada dated April 16, 2018 where it says that the "reviewers agreed that the MPL is not really an excipient since it is derived from a biologic (bacterial cell bank) and has biological activity," and indicate that it is apparent that "Health Canada considers that adjuvants with biological activity are not appropriately classified as regular non-medicinal excipients."

The April 16, 2018 email does not suggest or indicate that Health Canada considers adjuvants medicinal ingredients. Instead, the email dealt with the categorization of a post-NOC change, and Health Canada's response was based on the biological origin of the adjuvant component as well as the risk level associated with the change. Adjuvants are considered to be excipients in the context of the drug submission, but the level of data required for an adjuvant is greater than what is required for other excipients. It is in this context that Health Canada made the statement that "MPL is not really an excipient." However, the elevated level of data required to support an adjuvant component of biological origin, such as MPL, does not mean that Health Canada considers such an adjuvant a medicinal ingredient.

Finally, the World Health Organization's "Guidelines on the nonclinical evaluation of vaccine adjuvants and adjuvanted

vaccines" states on page 8 that regulatory agencies can provide a legal or regulatory classification for adjuvants:

> Many regulatory agencies, in addition to defining an adjuvant based on its immune-enhancing biological activity, provide a regulatory and/or legal classification for the adjuvant component of a vaccine (e.g., excipient, active ingredient or constituent material). It is possible that depending on the particular definition used by the regulatory authority, additional testing may be required. These regulatory and legal issues are specific for each regulatory authority and are beyond the scope of this document.

As is evident from the Vaccine Guidance Document, Health Canada has chosen to consider adjuvants as excipients, and not medicinal ingredients, within its regulatory framework.

While the TPD considers the question of whether or not an adjuvant is a medicinal ingredient as a regulatory question, we also note that you put forward a scientific argument in your representations. On page 6, you also submit that the $AS01_B$ adjuvant is biologically active, and that "[t]ogether, the adjuvant and the antigen are an immunogenic composition, responsible for activating the immune system response." Previously on page 5, you cited *Bayer Inc v Canada (Minister of Health)*, 2009 FC 1171 at paras 86-87, aff'd 2010 FCA 161, for the proposition that the term "medicinal ingredient" means the "substance in the formulation which, once administered, is responsible for the drug's desired effect in the body."

It is the position of the TPD that an adjuvant in a vaccine is not responsible for a vaccine's desired effect in the body. On page 11, the PM states that "SHINGRIX is designed to induce antigen-specific cellular and humoral immune responses in individuals with pre-existing immunity against varicella zoster virus (VZV)" (emphasis added). It is the VSV gE, the antigen in the vaccine, that induces this specific response, not the $AS01_B$ adjuvant, which only improves the response induced by the antigen. Administration of the adjuvant by itself would be incapable of inducing an antigen-specific cellular or humoral immune response related to the VZV, whereas administration of VSV gE in the absence of the adjuvant can induce such a response, even if it is negligible.

Health Canada considers adjuvants to be non-medicinal ingredients. The inconsistency in the treatment of some components of the adjuvant in SHINGRIX in the PM was introduced by GSK. In addition, the cited email relating to a different vaccine must be read in the context it was intended. In any event, any decisions related to past files are not relevant to the present case, and do not prevent the TPD from maintaining the position that adjuvants are non-medicinal ingredients.

…

There is no provision in subsection 3(2) of the *CSP Regulations* that permits an eligible patent to pertain to or claim a *composition* comprising a medicinal ingredient and *non-medicinal ingredients*, or uses of such compositions.

In your representations on page 5, you submit that there is not "any legislative reference to exclude certain types of claims from CSP eligibility because they claim both medicinal and non-medicinal ingredients."

The TPD disagrees. A claim does not pertain in the prescribed manner to a medicinal ingredient, or combination of medicinal ingredients, if it is a claim relating to a formulation, because a formulation includes non-medicinal ingredients in addition to the medicinal ingredient(s). Such a claim is outside the scope of the paragraphs of subsection 3(2) of the *CSP Regulations*, which do not allow for the presence of non-medicinal ingredients. The Regulatory Impact Analysis Statement ("RIAS") that accompanied the *CSP Regulations* further explains how a patent must pertain to the approved medicinal ingredient(s), and explicitly states that a claim directed to a formulation does not make a patent eligible for a CSP. The RIAS recites the following at page 10:

> ...an eligible patent need not protect the approved medicinal ingredient but must pertain to the *same* medicinal ingredient [see (a) above] as contained in the drug for which the authorization for sale specified on the CSP application was issued. To pertain to the *same* medicinal ingredient, the patent must include at least one claim that is directed at
>
> - the *same* medicinal ingredient;
> - any use of the *same* medicinal ingredient; or
> - the *same* medicinal ingredient as produced by a defined process (product-by-process).

> [...]
>
> Also, claims that are directed to a formulation containing the medicinal ingredient, including compositions, preparations or similar claim types, do not make a patent eligible for a CSP. A claim to a formulation does not protect the medicinal ingredient or combination of medicinal ingredients *per se*... This is consistent with CETA, which only requires the protection of the medicinal ingredient or combination of medicinal ingredients when claimed "as such".

In the quote above, the RIAS also describes how the exclusion of claims directed to a formation from eligibility is consistent with the Comprehensive Economic and Trade Agreement ("CETA"), which only requires the protection of the medicinal ingredient or combination of medicinal ingredients when claimed "as such."

The foregoing position is also reiterated in the Health Canada Guidance Document: *Certificate of Supplementary Protection Regulations* at page 17:

> A claim to a formulation does not protect the medicinal ingredient or combination of all the medicinal ingredients *per se* because claim to a formulation includes other elements in addition to the medicinal ingredient(s).

Claims 3 and 4 of the '905 patent also do not meet the requirements of subsection 3(2) of the *CSP Regulations* for another reason. Claims 3 and 4 both require that the gE antigen either comprises SEQ ID NO:1 (claim 3), or the gE antigen consists of SEQ ID NO:1 (claim 4). However, the sequence of the gE antigen as set out in section 3.2.S.1.2 Structure of the submission differs from SEQ ID NO:1 at positions 150 and 496 (as numbered in SEQ ID NO:1). As a result, claims 3 and 4 do not claim the medicinal ingredient or a use of the medicinal ingredient approved in SHINGRIX, rather they claim the use of a composition (claim 3) or a composition (claim 4) that includes a protein as defined in SEQ ID NO:1.

SHINGRIX contains a single medicinal ingredient: the gE antigen. The '905 patent does not claim the approved medicinal ingredient, the approved medicinal ingredient as obtained by a specified process or a use of the approved medicinal ingredient.

For all of the reasons provided above, CSP application No. 900006 is not eligible for a CSP.

[6] At the core of the Minister's decision is the position that, to be eligible for a CSP, a patent must include at least one claim limited to one or more medicinal ingredients, or to their use. According to this view, the 905 Patent is not so limited because each of the claims includes a non-medicinal ingredient (an adjuvant). The Minister says that because the 905 Patent claims are not limited to only medicinal ingredients, they amount to claims for a CSP-ineligible formulation.

[7] Central to the Minister's decision is the position that, notwithstanding the undisputed scientific evidence that the adjuvant used in SHINGRIX® is biologically active and essential to its clinical efficacy, the CSP eligibility provisions must be interpreted consistently with Health Canada's licensing guidelines which treat adjuvants, whether biologically active or not, as though they are inactive excipients.[1]

[8] It was also the Minister's position that because vaccine adjuvants do not independently initiate an immunological reaction they cannot be considered to be medicinal ingredients. Only the co-administered antigen fits that requirement because it triggers an immune response.

[1] The usual definition of a pharmaceutical excipient is an "inactive" substance often in the form of fillers, stabilizers, preservatives, and the like.

[9] The Minister's position was further explained by evidence given under cross-examination by Dr. Maria Baca-Estrada in the following exchange:

> 118 Q. At Paragraph 28 of your Affidavit, you explain that the "determination of whether a drug component is a medicinal or non-medicinal ingredient is not made based on whether the component has any biological activity".
>
> Correct?
>
> A. Yes, that's correct.
>
> 119 Q. But you would agree that the AS01B Adjuvant System contained in SHINGRIX does have a biological activity?
>
> A. As other adjuvants that we have had for decades -- and aluminum hydroxide is a good example. It is an excipient and is an adjuvant that has biological activity. Therefore, our position on the definition of excipients or adjuvants themselves is not necessarily based on the potential induction of a biological activity. Some adjuvant, some excipients, may have biological activity. Some others would not. So what I can say, as I mentioned here, is that the classification, the determination of whether a drug component is a medicinal or non-medicinal ingredient is not made based on the biological activity.
>
> I think that is an important point to make.
>
> 120 Q. At Paragraph 29 of your Affidavit, you state that "vaccine adjuvants do not independently contribute to the proposed use of the vaccine".
>
> Correct?
>
> A. I think that --
>
> Yes, it is correct that the adjuvant independently did not contribute, as any other excipient independently would not contribute to the Indication or the desired effect.
>
> So this is not just in this situation; this is related to excipients in general.

Excipients in general would not, of themselves, independently contribute to the Indication.

121 Q. Do all excipients have biological activity?

A. No, not all. Some do; some don't. It all depends on the excipient.

122 Q. Based on your statement at Paragraph 29 that "vaccine adjuvants do not independently contribute to the proposed use of the vaccine", I take it that it is your position that the AS0lB Adjuvant System contained in SHINGRIX does not independently contribute to the proposed use of the vaccine.

Is that fair?

A. I think the context of this paragraph is in line with the position that the key ingredient in a vaccine to excerpt the desired effect is the antigen. The rest of the excipients in a formulation contribute in different degrees, in different mechanisms, to the effect; as mentioned here, to the desired effect of the formulation. But the excipients themselves do not. Whether the excipients such as the ASO1B have, or not, biological activity.

And I think that is well --

That is our position that we have outlined in the Guidance document, where we have explicitly requested Sponsors to include all of the information on the adjuvant systems or excipients under the "Excipients" Section of the Submission.

And so in the context of what an excipient does to formulation, as I mentioned, it could/could not have a direct effect in the activity. The importance in a vaccine is that the medicinal ingredient, the antigen, is the one that is responsible for inducing the protection, the specific protection against disease.

And that is the context of what I included in Paragraph 29.

123 Q. Just circling back to my question, my question is: Would you agree that the ASO1B Adjuvant System contained in SHINGRIX does not independently contribute to the proposed use of the vaccine SHINGRIX?

A. Are you asking me: If I use ASO1B alone, would I have an immune response to the varicella zoster virus?

The answer is “No, you don’t”.

In itself, the adjuvant alone would not exert, in the context of SHINGRIX, an immune response that would be considered protective against the disease, the infection.

That is correct.

124 Q. So in combination with the gE antigen, the ASOlB Adjuvant System contained in SHINGRIX does contribute to the use of the vaccine; correct?

A. It would be the same as if----- (Short pause)

The same adjuvant, the ASO1, could also be used in combination with a different antigen for a different Indication.

In the case of the SHINGRIX, the final formulation was designed to exert an immune response against the medicinal ingredient, the gE antigen, which, in turn, protects the individual against the infection.

That is correct.

125 Q. So the ASO1B Adjuvant System in SHINGRIX, it is fair to say, increases the body’s immune response to the gE antigen?

A. The dose of antigen that is included in the final formulation for SHINGRIX --

It is noted that the adjuvant itself contributes to the enhancement of the immune response, at the dose of antigen used in the formulation.

[pp 1733-1737] [Emphasis added.]

III. Standard of Review

[10] Following the release of the Supreme Court of Canada decision in *Canada (Minister of Citizenship and Immigration) v Vavilov*, 2019 SCC 65, [2019] SCJ No 65 (QL) [*Vavilov*], the parties were invited to make further submissions on the standard of review to be applied to the Minister's decision.

[11] Although GSK acknowledges that the presumptive standard of reasonableness applies to the issues of statutory interpretation that were before the Minister, it continues to assert that correctness applies to the Minister's construction of the 905 Patent claims. Although this issue was not addressed in *Vavilov* and remains open for debate, it has no obvious application to this review of the Minister's decision. That is so because the decision did not turn on a disagreement about the meaning of the 905 Patent claims language. Rather, the question before the Minister was whether the adjuvant indisputably claimed in the 905 Patent is a "medicinal ingredient" as that term is used in the *Patent Act*, RSC 1985, c P-4, and in the *Certificate of Supplementary Protection Regulations*, SOR/2017-165 [*CSP Regulations*]. There is no disagreement about claims language *per se*, but there is a disagreement about Health Canada's regulatory classification of adjuvants as "non-medicinal ingredients" for the purposes of issuing a CSP to GSK. The Minister also did not disagree with GSK's evidence that the antigen and the adjuvant claimed by the 905 Patent were both biologically active and that the adjuvant was necessary to achieve clinical efficacy. Indeed, Dr. Baca-Estrada conceded that the adjuvant used in SHINGRIX® enhances the immune response and the Minister acknowledges on this application that the adjuvant has biological activity.

[12] GSK's attempt to categorize the disagreement as one of claims construction is also belied by its own supplementary submission at paragraph 68 where the "crux of the dispute" was said to lie in the meaning "medicinal ingredient in the relevant provisions". This, I think, more accurately frames the scope of this review and dictates that the applicable standard is "reasonableness" throughout.

[13] The decision in *Vavilov* does, however, offer considerable guidance about how reasonableness applies generally, and, more particularly, with respect to matters involving statutory interpretation. The focus of any judicial review begins with the reasons supplied by the decision-maker. Those reasons must be examined for their justification, intelligibility and transparency but with sensitivity to context: see *Vavilov*, above, at paras 88-90. A decision should only be set aside when the reviewing court is satisfied that it contains serious shortcomings that are sufficiently central or significant that the decision cannot stand.

[14] In the context of a matter where the determinative issue involves statutory interpretation, the impugned decision must comply with the rationale, purview, and specific constraints of the statutory scheme (*Vavilov*, para 108). In some cases, international law will be an important constraint on discretion even where the law has not been domestically implemented (*Vavilov*, para 114).

[15] In *Vavilov*, the Court emphasizes that administrative decision-makers must apply governing statutory language in accordance with the well-known modern principle of statutory interpretation. That is to say, that statutory language must be read in its entire context and in its

grammatical and ordinary sense harmoniously with the legislative scheme, the object of the legislation and the intention of Parliament (*Vavilov*, para 117, and *AstraZeneca v Canada (Minister of Health)*, 2006 SCC 49, [2006] 2 SCR 560 at para 38,). It is not open to a decision-maker to "disregard or rewrite the law enacted by Parliament" or to otherwise stray beyond the limits set by the statutory language under consideration (*Vavilov*, above, at paras 108 and 110). Where the words used are precise and unequivocal, their ordinary meaning will usually be a significant consideration (*Vavilov*, para 120). The Court concluded this part of the decision with the following observations:

> [121] The administrative decision maker's task is to interpret the contested provision in a manner consistent with the text, context and purpose, applying its particular insight into the statutory scheme at issue. It cannot adopt an interpretation it knows to be inferior — albeit plausible — merely because the interpretation in question appears to be available and is expedient. The decision maker's responsibility is to discern meaning and legislative intent, not to "reverse-engineer" a desired outcome.
>
> [122] It can happen that an administrative decision maker, in interpreting a statutory provision, fails entirely to consider a pertinent aspect of its text, context or purpose. Where such an omission is a minor aspect of the interpretive context, it is not likely to undermine the decision as a whole. It is well established that decision makers are not required "to explicitly address all possible shades of meaning" of a given provision: *Construction Labour Relations v. Driver Iron Inc.*, 2012 SCC 65, [2012] 3 S.C.R. 405, at para. 3. Just like judges, administrative decision makers may find it unnecessary to dwell on each and every signal of statutory intent in their reasons. In many cases, it may be necessary to touch upon only the most salient aspects of the text, context or purpose. If, however, it is clear that the administrative decision maker may well, had it considered a key element of a statutory provision's text, context or purpose, have arrived at a different result, its failure to consider that element would be indefensible, and unreasonable in the circumstances. Like other aspects of reasonableness review, omissions are not stand-alone grounds for judicial intervention: the key question is whether the omitted aspect of the analysis causes the reviewing court to lose confidence in the outcome reached by the decision maker.

[16] In upholding the Federal Court of Appeal Judgment setting aside a decision of the Canadian Registrar of Citizenship in *Vavilov*, the Court specifically noted the Registrar's failure to address the entirety of the applicable legislative scheme including other relevant legislation and international obligations, all of which informed the purpose of the provision being applied. The Registrar's review was described as "cursory" and the decision was not justified by the reasons given. This failure also gave rise to the potential for unintended and unjustified consequences in other factual contexts.

[17] It is against the above-noted considerations that the Minister's decision in this case must be reviewed. The onus, of course, is on GSK to establish that the Minister's decision was unreasonable.

IV. Analysis – Statutory Regime

[18] It is clear that the origins of Canada's CSP legislative regime lie in Chapter 20 of the Canada-European Union Comprehensive Economic Trade Agreement [CETA] dealing with supplementary patent-like protection for certain eligible pharmaceutical patents. The broad purposes of this form of supplementary protection are described in the following passages from the Regulatory Impact Analysis Statement supporting the *CSP Regulations*:

> The *Certificate of Supplementary Protection Regulations* (the Regulations) are required, in conjunction with amendments to the *Patent Act* in the *Canada-European Union Comprehensive Economic and Trade Agreement Implementation Act*, to establish an additional period of protection for drugs containing a new medicinal ingredient, or a new combination of medicinal ingredients, protected by an eligible patent. The legislative and

> regulatory changes are required to meet Canada's commitment under the Canada-European Union Comprehensive Economic and Trade Agreement (CETA).
>
> …
>
> In order to meet Canada's CETA obligations, the *Patent Act* (the Act) was amended to create a framework for the issuance and administration of certificates of supplementary protection (CSP), for which patentees with patents relating to human and veterinary drugs may apply. As set out in the Act, the new CSP regime, which will be administered by the Minister of Health (Minister), will provide additional protection from the date of the expiry of the eligible pharmaceutical patent based on the first authorization for sale of a drug containing a new medicinal ingredient or combination of medicinal ingredients in Canada. This new protection, which is intended to partly compensate for time spent in research and obtaining marketing authorization, provides patent-like rights in respect of drugs containing the same medicinal ingredient or combination. The scope of protection can be no broader than the scope of protection afforded by the patent set out in the CSP, and is subject to the same limitations and exceptions as the patent.
>
> …
>
> The Regulations accompany the Act amendments which establish the CSP regime. This regime implements Canada's commitment in the CETA by providing for an additional period of patent-like protection for drugs containing new medicinal ingredients and new combinations of medicinal ingredients.
>
> [Emphasis added]

[19] Statements similar to those above can be found in the Introduction to the Health Canada Guidance Document for the application of the *CSP Regulations* at Articles 1.1 and 1.2.

[20] Article 20.6 of CETA makes it clear that supplementary protection was intended to be available for eligible pharmaceutical patents covering a "vaccine" useful for "preventing disease".

[21] Under Article 20.27 of CETA, an eligible or so-called basic patent is one that protects "as such" an "active ingredient or combination of active ingredients" of, *inter alia*, a vaccine.

[22] The amendments to the *Patent Act*, RSC 1985, c P-4, intended to implement the CSP regime also apply to vaccines by including, in section 104, drugs useful in the "prevention of disease".

[23] The question presented to the Minister is whether the 905 Patent is eligible for supplementary protection. The Minister found that it was not eligible because the relevant 905 Patent claims do not protect a "medicinal ingredient" *per se*, but, rather, protect a combination of ingredients in the form of a single medicinal ingredient (i.e. an antigen) and a non-medicinal ingredient (i.e. an adjuvant). In other words, the 905 Patent claims a formulation and, as such, it is ineligible for a CSP. GSK disputes the Minister's characterization of the 905 Patent saying that both of the claimed ingredients (i.e. the antigen and the adjuvant) are medicinal in the sense that both are biologically active and the antigen will not produce the desired immune response without the adjuvant.

[24] In order to assess the reasonableness of the Minister's decision, consideration must be given to the patent eligibility requirements found in the *Patent Act* and in the *CSP Regulations* as informed by CETA. Under section 106 of the *Patent Act*, a CSP eligible patent is one that "pertains in the prescribed manner to a medicinal ingredient, or a combination of medicinal ingredients, contained in a drug for which the authorization for sale of the prescribed kind was

issued …". The *CSP Regulations* at section 3 further describe the "prescribed manner" in which a patent is deemed eligible for supplementary protection:

Certificate of Supplementary Protection Regulations, SOR/2017-165	***Règlement sur les certificats de protection supplémentaire***, DORS/2017-165
Eligible patents — requirement	**Brevets admissibles — exigence**
3 (1) For the purpose of paragraph 106(1)(a) of the Act, the prescribed requirement is that the patent must be in force.	3 (1) Pour l'application de l'alinéa 106(1)a) de la Loi, le brevet doit être en vigueur.
Eligible patents — manners of pertinence to medicinal ingredients	**Brevets admissibles — manières de lier aux ingrédients médicinaux**
(2) For the purpose of paragraph 106(1)(c) of the Act, the prescribed manners in which a patent may pertain to a medicinal ingredient or combination of medicinal ingredients are the following:	(2) Pour l'application de l'alinéa 106(1)c) de la Loi, le brevet est lié à un ingrédient médicinal ou à une combinaison d'ingrédients médicinaux de l'une ou l'autre des manières suivantes :
(a) the patent contains a claim for the medicinal ingredient or combination of all the medicinal ingredients contained in a drug for which the authorization for sale set out in the application for a certificate of supplementary protection was issued;	a) le brevet contient une revendication de l'ingrédient médicinal ou de la combinaison de tous les ingrédients médicinaux contenus dans une drogue pour laquelle l'autorisation de mise en marché mentionnée dans la demande de certificat de protection supplémentaire a été délivrée;
(b) the patent contains a claim for the medicinal ingredient or combination of all the medicinal	b) le brevet contient une revendication de l'ingrédient médicinal ou de la combinaison de tous

ingredients as obtained by a specified process and contained in a drug for which the authorization for sale set out in the application for a certificate of supplementary protection was issued; and	les ingrédients médicinaux tels qu'ils sont obtenus au moyen d'un procédé déterminé et tels qu'ils sont contenus dans une drogue pour laquelle l'autorisation de mise en marché mentionnée dans la demande de certificat de protection supplémentaire a été délivrée;
(c) the patent contains a claim for a use of the medicinal ingredient or combination of all the medicinal ingredients contained in a drug for which the authorization for sale set out in the application for a certificate of supplementary protection was issued.	c) le brevet contient une revendication d'une utilisation de l'ingrédient médicinal ou de la combinaison de tous les ingrédients médicinaux contenus dans une drogue pour laquelle l'autorisation de mise en marché mentionnée dans la demande de certificat de protection supplémentaire a été délivrée.
[Emphasis added]	[soulignement ajouté]

[25] The primary basis for refusing a CSP for the 905 Patent can be found in the Regulatory Impact Analysis Statement [RIAS] at page 10 which purports to exclude eligibility for patent claims directed to the protection of pure processes or formulations. That analysis provides:

A patent which protects more than one medicinal ingredient or more than one combination of medicinal ingredients, subject to the rules on variations and combinations, would be eligible to support a CSP application in respect of each of those medicinal ingredients or combinations, as the case may be. However,	Un brevet qui protège plus d'un ingrédient médicinal ou plus d'une combinaison d'ingrédients médicinaux, sous réserve des règles relatives aux variations et aux combinaisons, serait admissible au soutien d'une demande de CPS relativement, selon le cas, à chacun des ingrédients médicinaux ou à

pure process claims do not protect the product and therefore do not render a patent eligible for a CSP.	chacune des combinaisons d'ingrédients médicinaux. Cependant, les revendications au titre d'un processus pur ne protègent pas le produit et, par conséquent, ne rendent pas un brevet admissible à un CPS.
Also, claims that are directed to a formulation containing the medicinal ingredient, including compositions, preparations or similar claim types, do not make a patent eligible for a CSP. A claim to a formulation does not protect the medicinal ingredients or combination of medicinal ingredients *per se*. A claim to a formulation may be directed, for example, to the improvement of the stability of medicinal ingredients. This is consistent with CETA, which only requires the protection of the medicinal ingredient or combination of medicinal ingredients when claimed "as such."	De plus, les revendications qui visent une formulation contenant l'ingrédient médicinal, y compris les compositions, les préparations ou des revendications similaires, ne rendent pas un brevet admissible à un CPS. Une revendication relative à une formulation ne protège pas l'ingrédient médicinal ou la combinaison d'ingrédients médicinaux en soit. Par exemple, une revendication à l'égard d'une formulation peut être orientée vers l'amélioration de la stabilité des ingrédients médicinaux. Cela est conforme avec l'AECG, qui ne requiert que la protection de l'ingrédient médicinal ou de la combinaison d'ingrédients médicinaux lorsqu'ils sont revendiqués « comme tels ».

[26] It is noteworthy that there is nothing in the relevant *Patent Act* CSP provisions or in the *CSP Regulations* that expressly supports a requirement that an eligible claim is one that protects a medicinal ingredient or a combination of medicinal ingredients *per se*. Although CETA defines an eligible patent (i.e. a basic patent) as one that protects a "product as such", it also defines the protected product as "the active ingredient or combination of active ingredients" in

the approved drug or vaccine (see CETA, Article 20.6). CETA does not refer at all to "medicinal ingredients" and nowhere in Canadian legislation is that term defined.

[27] The absence of any statutory definition for "medicinal ingredient" is significant because the *Canada-European Union Comprehensive Economic and Trade Agreement Implementation Act*, SC 2017, c 6 [*CETA Act*] at section 3 directs that, unless otherwise stipulated, matters of statutory interpretation are to be resolved harmoniously with CETA. That provision provides:

Interpretation consistent with Agreement	**Interprétation compatible**
3 For greater certainty, this Act and any federal law that implements a provision of the Agreement or fulfils an obligation of the Government of Canada under the Agreement is to be interpreted in a manner consistent with the Agreement.	3 Il est entendu que la présente loi et tout texte législatif fédéral qui met en oeuvre une disposition de l'Accord ou vise à permettre au gouvernement du Canada d'exécuter une obligation contractée par lui aux termes de l'Accord s'interprètent d'une manière compatible avec celui-ci.

[28] To the extent that the applicable Canadian CSP legislation is open to interpretation, this provision calls for interpretive consistency with the language of CETA and not necessarily with Health Canada's drug licensing guidelines.

V. Purposive Approach

[29] It was incumbent on the Minister to adopt a purposive approach to the interpretation of the CSP amendments to the *Patent Act* and of the *CSP Regulations*. This required the Minister to consider the broad purposes of the legislative scheme having due regard to what was intended

under CETA. Clearly, CETA contemplated the grant of supplemental protection to inventive vaccines. There is also no dispute that vaccines often require both an antigen and an adjuvant to be effective. Indeed, the inventive aspect of a vaccine patent may well lie in the discovery of a novel combination of a known antigen with a known adjuvant. The question the Minister needed to consider was whether the perceived need for administrative consistency was a reasonable basis to deny a CSP to GSK for its 905 Patent.

[30] At paragraph 80 of the Minister's Memorandum of Fact and Law, the argument is made that the absence of a definition of "medicinal ingredient" in the *Patent Act*, *CSP Regulations*, *Food and Drug Regulations*, CRC, c 870 or *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133 affords the Minister greater interpretive latitude. At the same time, the Minister concedes that "medicinal ingredient" means "the substance in the formulation which, once administered, is responsible for the drug's desired effect in the body": see *Bayer Inc v Canada*, 2009 FC 1171 at paras 86-87 aff'd 2010 FCA 161, [2009] FCJ No 1471. According to the Minister's decision "an adjuvant in a vaccine is not responsible for a vaccine's desired effect in the body" because, unlike the antigen, it does not <u>independently</u> trigger an immune response.

[31] This point was further clarified in Dr. Baca-Estrada's affidavit at paras 26-29:

> 26. The HPFB considers vaccine antigens to be medicinal ingredients, and all vaccine adjuvants and their components to be excipients, which are non-medicinal ingredients. I and the BGTD representatives confirmed the HPFB's position at the July 12, 2018 meeting.
>
> 27. In addition to the HPFB's position that adjuvants are considered to be "non-medicinal ingredients" as set out in the Health Canada Vaccine Guidance, we also discussed the arguments in GSK's Representations related to the biological activity of some adjuvant components.

> 28. As we discussed in the July 12, 2018 meeting, the determination of whether a drug component is a medicinal or non-medicinal ingredient is not made based on whether the component has any biological activity. Instead, as set out in Health Canada's "Guidance for Completing the Drug Submission Application Form" in its explanation of the "medicinal (active) ingredient(s)" (item 56), the medicinal ingredients are those "that contribute to the proposed use of the product." A copy of Health Canada's "Guidance for Completing the Drug Submission Application Form" is attached as Exhibit "E".
>
> 29. In the case of a vaccine, the use is the protection against future infections through recognition of the antigen if the pathogen is encountered again. In contrast, vaccine adjuvants do not independently contribute to the proposed use of the vaccine. With only an adjuvant (and no antigen), the immune system has nothing from the pathogen to, for example, produce antibodies against. Without the production of antibodies specific to the antigen, there are no antibodies to help protect against future infections by the recognition of the antigen if the pathogen is encountered again. Instead, adjuvants must be used in association with an antigen, because adjuvants only increase the body's immune response to an antigen.
>
> [Emphasis added.]

[32] According to the Minister, a vaccine adjuvant can never be a medicinal ingredient, whatever its biological activity may be and regardless of its significance in achieving a desired clinical response. It was, of course, open to the Minister to adopt a more expansive interpretation of medicinal ingredient in cases where an adjuvant enhances the biological response initiated by the vaccine antigen and where the adjuvant is essential to achieving the desired therapeutic effect. The question that remains is whether the Minister's decision to restrict the definition of "medicinal ingredient" was reasonable, having due regard to the statutory purpose and language of the CSP regime.

[33] In my view, the Minister's decision is not justified by the reasons provided. The fundamental deficiency in the Minister's reasoning stems from the adoption of administrative tunnel vision to the exclusion of several highly relevant considerations.

[34] What the Minister failed to consider was the statutory requirement in s 3 of the *CETA Act* that the interpretation of Canadian law implementing CETA was to be done "in a manner consistent with the [CETA] Agreement". Inasmuch as the term "medicinal ingredient" was open to interpretation, the Minister was, therefore, required to consider and apply the language of CETA. Article 20.27 of CETA Agreement defines a protected product as "the active ingredient or combination of active ingredients" of an authorized pharmaceutical product (i.e. SHINGRIX®).

[35] According to this language in CETA, biological activity was the measure by which CSP relief was to be made available in Canada. This is also consistent with Health Canada's own Guidance for Completing the Drug Submission Application Form at page 16, Article 56 which calls upon a proponent to list "the medicinal (active) ingredients that contribute to the proposed use of the product". Although in other places and for apparently administrative reasons, Health Canada classifies vaccine adjuvants as excipients, that approach has no obvious application to the purposes served by CETA.

[36] Indeed, there is no obvious rationale to support the argument at paragraph 86 of the Minister's Memorandum of Fact and Law that it would be unreasonable to adopt an incongruent practice of considering adjuvant components as non-medicinal ingredients for Notice of

Compliance [NOC] purposes but as medicinal ingredients for CSP purposes. The fact that the Minister obtains some degree of administrative efficiency by treating vaccine adjuvants as though they are excipients for licensing purposes does not dictate or inform the legal obligations that pertain to extending patent-like protection for an already approved drug.

[37] The Minister's further argument on this application, that GSK's claim to relief represents a collateral attack on the decision to issue a NOC for SHINGRIX®, has no merit. The grant of a CSP to GSK would not somehow undermine the NOC authorizing the sale of SHINGRIX®. A CSP simply extends additional exclusivity for the drug in Canada. Furthermore, the fact that GSK, for certain regulatory purposes, listed the antigen as the only active ingredient in SHINGRIX® does not create an estoppel. This approach was presumably in keeping with the Minister's administrative approach to treating adjuvants as excipients for filing and some notification purposes. The fact that the Minister uses this administrative shortcut does not mean that this guidance to industry is somehow legally binding for the purposes of applying the CSP regime or that the scientific facts behind each CSP submission can be effectively ignored.

[38] It is also of concern that the Minister's decision offers no justification for adding the requirement that vaccine adjuvants do not qualify as medicinal ingredients because they do not independently cause an immune response. Presumably the desired effect in the body is a clinically meaningful effect and not a negligible immune response that the administration of the antigen alone would prompt. I agree with GSK's argument that there is an apparent logical fallacy to the Minister's position that a "medicinal ingredient" must independently contribute to achieving the desired effect (i.e. the immunological response) in the body. That is so because, as

the evidence shows, neither the antigen nor the adjuvant on their own could be said to provoke a clinically useful response. Taken to its logical conclusion, the Minister's position would disqualify the antigen as a medicinal ingredient because it has, by itself, no clinical value. This, of course, would be an illogical result that effectively extinguishes the words "desired effect in the body" from the agreed definition of "medicinal ingredient".

[39] If the Minister's position were to be applied uniformly, any new and useful vaccine that requires an adjuvant to be effective would be excluded for supplementary protection based on Health Canada's administrative classification of adjuvants as excipients. Inasmuch as many useful vaccines are adjuvanted and patented as such, this would exclude CSP protection for many novel vaccines. It is at least doubtful that such a result was intended by CETA. This is the kind of anomaly that was of concern in *Vavilov*, above, and it should have been addressed by the Minister.

[40] Added to all of this is the fact that Health Canada does not consistently treat vaccine adjuvants as excipients for all purposes. For instance, in the case of SHINGRIX®, Health Canada accepted GSK's Patent List of the 905 Patent which listed both the antigen and the adjuvant as medicinal ingredients (Applicant's Record, p 0091). Similarly, it approved GSK's product monograph for SHINGRIX® which stated that the adjuvant system is part of the vaccine's "mechanism of action".

[41] In another example, Health Canada acknowledged that for purposes of a post-NOC change notification, GSK's adjuvant for its Cervarix™ vaccine "is not really an excipient"

because it had biological activity (Applicant's Record, p 0251). The related guidance document also separately defines "adjuvants" as a "component that potentiates the immune responses to an antigen and/or modulates it towards the desired immune responses" from "excipients", which are "anything other than the drug substance in the doseage form". Health Canada has also established a separate notification protocol for changes to adjuvants which, in some cases, may necessitate the filing of a new drug submission (Applicant's Record, p 0306). Indeed, the Minister's decision recognized that an adjuvant change may require additional supporting data because of the potential of greater patient risk.

[42] The Minister's decision also drew support from the World Health Organization's vaccine guidance which recognizes that member agencies may choose to classify adjuvants differently for regulatory purposes, including a requirement for additional testing. This guidance is in keeping with Health Canada's testing protocols, but it provides doubtful support for avoiding a commitment made in CETA with respect to extending patent-like protection to an already approved drug.

[43] The fact that Health Canada chooses for administrative reasons to categorize vaccine adjuvants as excipients and to treat them for licensing purposes in the same way as stabilizers, fillers and preservatives does not alter the scientific fact that the adjuvant in SHINGRIX® is an active and necessary ingredient of the medicine. Apart from a desire for supposed linguistic consistency, there is no apparent practical purpose served by excluding adjuvanted vaccines from the CSP regime – a regime that serves very different purposes than those that apply to pharmaceutical licensing: see section 7 of *CETA Act.*

[44] There is also nothing in the CSP provisions of the *Patent Act* or in the *CSP Regulations* that expressly excludes from eligibility patent claims directed to a formulation. The applicable provisions only require that the patent contain a claim for the medicinal ingredient included in a drug authorized for sale under a Notice of Compliance. It is only in the RIAS that the formulation exclusion appears and there the example given concerns a claim for an improvement to the stability of a known medicinal ingredient. The eligibility limitation that Health Canada reads into the *CSP Regulations* makes some sense to the extent that it is employed to prevent forms of evergreening. Claimed improvements consisting of minor variations that do not affect the performance of the active ingredient *per se* were presumably not intended to be eligible. However, the disqualification of a novel and useful vaccine on the basis that it is made-up from a unique and necessary combination of two biologically active components is hard to justify where the applicable regulations do not expressly and clearly apply and where the language of CETA suggests otherwise.

[45] The RIAS also indicates that the *CSP Regulations* are intended to implement Canada's commitment to CETA "by providing for an additional period of patent-like protection for drugs containing new medicinal ingredients and new combinations of medicinal ingredients". No where is it suggested that Canada was departing from the CETA commitment to protect "active ingredients". What the RIAS does indicate is an intention to exclude from protection patents that contain minor variations to known or off-patent compounds or their uses. That concern has no application to a vaccine like SHINGRIX®.

[46] Notwithstanding the concerns expressed above, this is not an appropriate case to direct the Minister to issue a CSP to GSK. The decision is set aside as unreasonable because it failed to take appropriate account of Canada's CETA commitments and the full scope and purposes of the applicable statutory provisions, most notably Article 20.27 of CETA and s 3 of the *CETA Act*. The matter is to be redetermined on the merits and in accordance with these reasons.

[47] I will reserve on the issue of costs. If the parties cannot agree on costs, I will receive further submissions in writing to be filed within 45 days and not to exceed 15 pages in length.

JUDGMENT IN T-1603-18

THIS COURT'S JUDGMENT is that this application is allowed with the matter to be redetermined on the merits and in accordance with the above reasons.

THIS COURT'S FURTHER JUDGMENT is that the issue of costs is reserved pending either agreement by the parties or the receipt of further written submissions within 45 days.

"R.L. Barnes"

Judge

FEDERAL COURT

SOLICITORS OF RECORD

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