Citation: Lee, Eng H. (Re), 2023 CACP 21
Commissioner's Decision 1654
Décision du commissaire nº1654
Date: 2023-07-18

TOPIC:	G00	Utility
	C00	Disclosure – Adequacy of Description
	J80	Subject matter of Applications – Professional or Artistic Skills
	O00	Obviousness - Obviousness

SUJET:	G00	Utilité
	C00	Divulgation – Caractère adéquat ou inadéquat de la description
	J80	Objet des demandes – Aptitude professionnelles (artistiques)
	O00	Évidence - Évidence

Application No. 2822924
Demande nº 2 822 924

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,822,924, having been rejected under subsection 199(1) of the *Patent Rules* (SOR/2019-251) has consequently been reviewed in accordance with paragraph 86(7)(c) of the *Patent Rules*. The recommendation of the Patent Appeal Board and the decision of the Commissioner are to refuse the application.

Agent for the Applicant:

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INTRODUCTION

[1] This recommendation concerns the review of rejected Canadian application number 2,822,924, which is entitled “Roadmap for controlling malaria” and is owned by Eng Hong Lee (the Applicant).

[2] A review of the rejected application has been conducted by the Patent Appeal Board (the Board) pursuant to paragraph 86(7)(c) of the *Patent Rules* (SOR/2019-251). As explained in more detail below, our recommendation is that the Commissioner of Patents refuse the application.

BACKGROUND

The application

[3] The application has a filing date of December 20, 2011 and was laid open to public inspection on July 5, 2012.

[4] The application relates to the use of a live low dose malaria vaccine consisting of at least five *Plasmodium* infected mosquitoes in a container to vaccinate a human or multiple humans in a target population on each of two or three consecutive days for preventing malaria.

[5] The claims under review are claims 1 to 14 on file, dated July 22, 2019 (the claims on file).

Prosecution history

[6] On August 4, 2020, a Final Action (FA) rejecting the claims on file was issued pursuant to subsection 86(5) of the *Patent Rules*. The FA stated that claims 1-14 were rejected for lacking utility contrary to section 2 of the *Patent Act* and for lacking support contrary to section 84 of the former *Patent Rules* (SOR/96-423, now section 60 of the *Patent Rules*) and further rejecting the description, insofar

as it relates to claims 1-14, for lacking an enabling disclosure contrary to subsection 27(3) of the *Patent Act*.

[7] In a November 6, 2020 response to the FA (RFA) the Applicant provided arguments in favour of the patentability of the claims on file. On December 4, 2020 the Applicant provided a supplemental response to the FA (SRFA) with further arguments in favour of the patentability of the claims on file. No claim amendments were proposed with either response.

[8] The Examiner was not persuaded by the arguments provided in the RFA and SRFA and so the application was forwarded to the Board for review on January 14, 2021 along with an explanation outlined in a Summary of Reasons (SOR).

[9] The SOR was forwarded to the Applicant on January 19, 2021. In a response dated March 1, 2021, the Applicant expressed continued interest in having the application reviewed by the Board.

[10] This Panel was formed to review the rejected application and make a recommendation to the Commissioner as to its disposition.

[11] In a preliminary review (PR) letter dated February 15, 2023 we set out our preliminary views that the subject-matter of claims 1-14 on file lacks utility but that the claims and description comply with section 60 of the *Patent Rules* and subsection 27(3) of the *Patent Act*, respectively. In our letter, the Applicant was notified in accordance with subsection 86(9) of the *Patent Rules* that an additional issue arose during our review regarding whether claims 5 and 6 are directed to methods of medical treatment. We provided a preliminary analysis of that issue and expressed our preliminary view that claims 5 and 6 equate to methods of medical treatment that are excluded from the definition of “invention” in section 2 of the *Patent Act*. Finally, we invited the Applicant to make oral and written submissions in response to our PR letter.

[12] In a phone call on March 10, 2023 the Applicant confirmed that they did not wish to have an oral hearing and that written submissions were forthcoming. Those written submissions were received with the response to our PR letter (RPR letter)

dated March 15, 2023 wherein the Applicant proposed amending the claims on file to proposed claims 1-21 and provided arguments in support of the patentability of those newly proposed claims.

[13] We have completed our review and have set out our conclusions below.

THE ISSUES ARE LACK OF UTILITY, LACK OF SUPPORT, LACK OF ENABLEMENT AND LACK OF PATENTABLE SUBJECT-MATTER

[14] This review considers whether the subject-matter of claims 1-14 on file at the time of the FA lacks utility; whether those claims are fully supported by the description; whether the description, insofar as it relates to claims 1-14, provides an enabling disclosure; and whether claims 5 and 6 comprise a method of medical treatment.

LEGAL PRINCIPLES AND OFFICE PRACTICE

Purposive construction

[15] In accordance with *Free World Trust v Électro Santé Inc*, 2000 SCC 66 and *Whirlpool Corp v Camco Inc*, 2000 SCC 67, purposive construction is performed from the point of view of the person skilled in the art in light of the relevant common general knowledge (CGK), considering the whole of the disclosure including the specification and drawings. In addition to interpreting the meaning of the terms of a claim, purposive construction distinguishes the essential elements of the claim from the non-essential elements. Whether or not an element is essential depends on the intent expressed in or inferred from the claim, and on whether it would have been obvious to the skilled person that a variant has a material effect upon the way the invention works.

[16] We consider that all elements set out in a claim are presumed essential unless it is established otherwise or where such a presumption is contrary to the claim language.

Utility

[17] Utility is required by section 2 of the *Patent Act*:

> **invention** means any new and useful art, process, machine, manufacture or composition of matter, or any new and useful improvement in any art, process, machine, manufacture or composition of matter.

[18] In *AstraZeneca Canada Inc v Apotex Inc*, 2017 SCC 36 at para 53 [*AstraZeneca*], the Supreme Court of Canada stated that the "[u]tility will differ based on the subject-matter of the invention as identified by claims construction" and outlined the approach that should be undertaken to determine whether a patent discloses an invention with sufficient utility under section 2 of the *Patent Act*:

> [54] To determine whether a patent discloses an invention with sufficient utility under s. 2, courts should undertake the following analysis. First, courts must identify the subject-matter of the invention as claimed in the patent. Second, courts must ask whether that subject-matter is useful—is it capable of a practical purpose (i.e. an actual result)?
>
> [55] The Act does not prescribe the degree or quantum of usefulness required, or that every potential use be realized—a scintilla of utility will do. A single use related to the nature of the subject-matter is sufficient, and the utility must be established by either demonstration or sound prediction as of the filing date (*AZT*, at para 56).

[19] Therefore, utility must be established either by demonstration or sound prediction as of the Canadian filing date. Utility cannot be supported by evidence and knowledge that only became available after this date (see also *Apotex Inc v Wellcome Foundation Ltd*, 2002 SCC 77 at para 56 [*AZT*], cited in the passage above).

[20] The doctrine of sound prediction allows the establishment of asserted utility even where that utility had not been fully verified as of the filing date. However, a patent application must provide a "solid teaching" of the claimed invention as opposed to "mere speculation" (*AZT* at para 69).

[21] The soundness of a prediction is a question of fact (*AZT* at para 71). Analysis of that soundness should consider three components (*AZT* at para 70):

- there must be a factual basis for the prediction;
- the inventor must have, at the date of patent, an articulable and sound line of reasoning from which the desired result can be inferred from the factual basis; and
- there must be a proper disclosure of the factual basis and line of reasoning.

[22] These components are assessed from the perspective of the skilled person to whom the patent is directed, taking into account their CGK. Further, with the exception of the CGK, the factual basis and line of reasoning must be included in the patent application (See *Bell Helicopter Textron Canada Ltée v Eurocopter SAS*, 2013 FCA 219 at paras 152–153 [*Bell Helicopter*]).

[23] Although a prediction does not need to amount to a certainty to be sound, there must be a *prima facie* reasonable inference of utility (*Gilead Sciences Inc v Idenix Pharmaceuticals Inc*, 2015 FC 1156 at para 251; *Mylan Pharmaceuticals ULC v Eli Lilly Canada Inc*, 2016 FCA 119 at para 55).

Lack of support

[24] Section 60 of the *Patent Rules* (equivalent to section 84 of the former *Rules*) states:

> The claims must be clear and concise and must be fully supported by the description independently of any document referred to in the description.

[25] We note that there is little judicial guidance on the requirements of that section, or any of its predecessor equivalents. The *Manual of Patent Office Practice* [MOPOP] section 16.05 (CIPO, October 2019) states:

> A claim must be fully supported by the description as required by section 60 of the *Patent Rules*. All the characteristics of the embodiment of the invention which

> are set forth in the claim must be fully set forth in the description (Section 60 of the *Patent Rules*)…
>
> A claim is objected to for lack of support by the description if the terms used in the claim are not used in the description and cannot be clearly inferred from the description.

Lack of enablement

[26] Subsection 27(3) of the *Patent Act* requires, among other things, a specification of a patent to correctly and fully describe an invention, and to enable its practice:

> 27(3) The specification of an invention must:
>
> (a) correctly and fully describe the invention and its operation or use as contemplated by the inventor;
>
> (b) set out clearly the various steps in a process, or the method of constructing, making, compounding or using a machine, manufacture or composition of matter, in such full, clear, concise and exact terms as to enable any person skilled in the art or science to which it pertains, or with which it is most closely connected, to make, construct, compound or use it;
> …

[27] A determination of whether the specification complies with paragraphs 27(3)(a) and 27(3)(b) of the *Patent Act* requires that three questions be answered: What is the invention? How does it work? Having only the specification, can the person of skill in the art produce the invention using only the instructions contained in the disclosure? see: *Teva Canada Ltd v Novartis AG*, 2013 FC 141 citing *Teva Canada Ltd v Pfizer Canada Inc*, 2012 SCC 60 [T*eva*] and *Consolboard v MacMillan Bloedel (Sask) Ltd*, [1981] 1 SCR 504 at 520 [*Consolboard*].

[28] With respect to this third question, “it is necessary that no additional inventive ingenuity be required in order to make the patent work” (*Aventis Pharma Inc v Apotex Inc*, 2005 FC 1283 at para 172). A patent will not be invalid for insufficient disclosure where routine experimentation is required of the skilled person, but the

Supreme Court of Canada has held that a disclosure is insufficient if the specification "necessitates the working out of a problem" (*Idenix Pharmaceuticals, Inc v Gilead Pharmasset LLC*, 2017 FCA 161 at para 19, citing *Pioneer Hi-Bred v Canada* [1989] 1 SCR 1623 at 1641).

Patentable subject-matter: methods of medical treatment

[29] The definition of invention is set out in section 2 of the *Patent Act*:

> **invention** means any new and useful art, process, machine, manufacture or composition of matter, or any new and useful improvement in any art, process, machine, manufacture or composition of matter.

[30] It is well established that methods of medical treatment and surgery are not patentable subject-matter falling within the manual and productive arts and are excluded from the definition of invention as defined in section 2 of the *Patent Act* (see *Tennessee Eastman Co v Commissioner of Patents* (1970), 62 CPR 117 (Ex Ct), aff'd [1974] SCR 111). However, medical "use" claims have been considered to be directed to patentable subject-matter (see AZT).

[31] With particular reference to the determination of patentable subject-matter in respect of medical use claims containing active medical treatment steps, the current Patent notice titled "Patentable Subject-Matter under the *Patent Act*"[1] states that:

> Where an actual invention includes one or more essential elements that comprise an active medical treatment step or surgical step or that restrict, prevent, interfere with, or require the exercise of the professional skill and judgment of a medical professional, the actual invention is an excluded method of medical treatment and is not patentable subject-matter.

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[1] https://ised-isde.canada.ca/site/canadian-intellectual-property-office/en/patents/patent-notices/patentable-subject-matter-under-patent-act

ANALYSIS

Purposive construction

[32] The claims on file contain claims 1-14. Claims 1-4 are the only independent claims. Claims 1 and 2 are illustrative:

> 1. Use of a live low dose malaria vaccine consisting of at least five *Plasmodium* infected mosquitoes in a container to vaccinate each human in a human target population on each of two consecutive days for preventing malaria.
>
> 2. A live low dose malaria vaccine consisting of at least five *Plasmodium* infected mosquitoes in a container for use to vaccinate each human in a human target population on each of two consecutive days for preventing malaria.

[33] Independent claims 3 and 4 are identical to claims 2 and 1, respectively, except that the vaccine is used to vaccinate a single human, rather than each human in a target population.

[34] Dependent claims 5-14 define further limitations relating to dosing on a third consecutive day (claims 5, 6), the *Plasmodium* strain (claims 7-12) and the minimum number of mosquito bites (claims 13, 14).

The person skilled in the art

[35] In our PR letter we said the following on page 8:

> In the Office letter of January 22, 2019, the skilled person is formally characterized as a scientist with a background in immunology and microbiology. The Applicant did not dispute this characterization. We agree that this is reasonable and, in our preliminary view, the skilled person or team would also have a background and expertise relating to vaccine development and would be familiar with the experimental malaria vaccines in development and commonly used antimalarial agents.

> Subject to any comments or clarifications the Applicant wishes to make, we intend to adopt the above characterization for the purposes of our analysis.

[36] In the RPR letter the Applicant did not dispute or contest our characterization and added that the skilled person would further possess experience in conducting vaccination experiments and interpreting the results (page 2):

> Such a scientist would possess research experience and experience in conducting vaccination experiments as well as analyzing the results obtained.

[37] We agree that this is reasonable and adopt this along with our characterization set out above for our analysis.

The common general knowledge of the skilled person

[38] In our PR letter we agreed with the Applicant's submissions in the RFA that the following information was part of the CGK (pages 8-9):

> …the Applicant asserts that the teachings of Roestenberg[2] (referred to on the record as document D3) and Epstein et al.[3] represent the CGK in the art at the time the present application was filed (page 5, RFA). Notably, both documents are discussed in the application.
>
> The RFA further contends that vaccinating people against malaria using live *Plasmodium*-infected mosquitoes was well-known and that it was CGK that 100% vaccination efficacy had been achieved by repeated dosing using mosquitoes in D3. The SOR does not dispute either of these contentions.
>
> D3 is a journal article disclosing the results of a successful clinical vaccine trial using live non-attenuated *Plasmodium* and chloroquine in human subjects. Subjects were

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[2] Roestenberg M et al, "Protection against a malaria challenge by sporozoite inoculation" (2009) 361:5 N Engl J Med 468-477 (D3)

[3] Epstein J et al, "Safety and clinical outcome of experimental challenge of human volunteers with *Plasmodium falciparum*-infected mosquitoes: an update" (2007) 196:1 J Infect Dis 145-154

exposed to bites from 12-15 mosquitoes infected with chloroquine-sensitive *Plasmodium falciparum* (*P. falciparum*) on three occasions separated by one month (i.e., once per cycle), while receiving chloroquine. Chloroquine was used because it is lethal to the blood-stage parasites that cause symptoms and disease but has no effect on the pre-blood stage forms.

After a washout period to clear the body of chloroquine, the subjects were challenged with a dose of 5 bites from *P. falciparum*-infected mosquitoes and were found to be 100% protected against infection. Specifically, no parasites were detectable in peripheral blood by microscope or by the more sensitive polymerase chain reaction (PCR) technique. The authors describe this as a proof-of-concept study that was designed to test whether the same success achieved by inoculating rodents with live non-attenuated *Plasmodium* (with concomitant chloroquine treatment) could be achieved in humans.

Epstein et al. is a review article comparing 18 different studies that used the bites of *P. falciparum*-infected mosquitoes as an experimental challenge to test if an antimalarial or previously administered vaccine regimen worked to prevent malaria. Epstein et al. reported that 5 mosquito bites provided an infectious dose of *P. falciparum* 100% of the time in control subjects.

In our preliminary view, since D3 discloses the results of a successful human trial of a live non-attenuated malaria vaccine, we agree with the RFA that it is reasonable that these teachings would have been CGK as of the filing date. We further agree with the RFA that it is reasonable that the teachings in Epstein et al., a review article summarizing results and trends from 18 different studies using the common mosquito bite challenge technique, would have been well-known to the skilled person.

[39] We also expressed our preliminary agreement with the FA that knowledge of the apicomplexan parasites *Plasmodium* and *Eimeria* that cause malaria and coccidiosis, respectively, would have been part of the CGK.

[40] On page 2 of the RPR letter, the Applicant agreed that a scientist with a background in microbiology would have knowledge of apicomplexan parasites *Plasmodium* and *Eimeria*.

[41] In our PR letter we also expressed our preliminary view that it was not CGK to the skilled person that testing an *Eimeria* vaccine in a chicken model was an appropriate surrogate for investigating efficacy and dosing of a live *Plasmodium* vaccine in humans: (pages 9-15, full citations provided in the PR letter)

> …the FA and SOR disagree with the Applicant's contention that it was CGK to use *Eimeria*, the parasite that causes coccidiosis in poultry, as a surrogate for studying *Plasmodium* vaccines: FA, page 4, in response to the Applicant's letter of July 22, 2019 (emphasis in the original)
>
> > While apicomplexan parasites have some similarities and *Eimeria* may be used for the general understanding of other apicomplexan microorganisms, it is not common general knowledge that Eimeria can be used as a surrogate <u>for vaccine development</u> for *Plasmodium* or any other apicomplexan microorganism.
>
> The principles governing the assessment of CGK were stated in *Eli Lilly & Co v Apotex Inc*, 2009 FC 991 at para 97 [*Lilly*], upheld by 2010 FCA 240, citing *General Tire & Rubber Co v Firestone Tyre & Rubber Co Ltd*, [1972] RPC 457, [1971] FSR 417 (UKCA) at pages 482 and 483 (of RPC). In sum, CGK is a concept derived from a common sense approach to the practical question of what would in fact be known to an appropriately skilled addressee. Generally, scientific articles form part of the CGK provided they are generally known and generally regarded as a basis for further action by the bulk of those who are engaged in a particular art.
>
> Established reference works (such as textbooks, review articles, handbooks, etc.) or demonstrated commonality of certain knowledge in a number of disclosures in the field are relevant to the inquiry: (see *MOPOP* at § 12.02.02c).
>
> Having in mind these principles, it is our view that the relevant question is whether information was generally known and accepted without question by the bulk of those who are engaged in the fields relevant to controlling human malaria, vaccine development and microbiology at the relevant time.
>
> …

With respect to using an *Eimeria* vaccine as a model for developing a human vaccine using live *Plasmodium* parasites, the RFA points to para 32 in the description which states the following (emphasis added):

> ***Eimeria* vaccines are an appropriate surrogate for studying *Plasmodium* vaccines for a number of reasons.** *Eimeria* and *Plasmodium* are both apicomplexan protozoan parasites: they are very closely related organisms…Importantly, for *Plasmodium*, *Eimeria* is the most closely related organism for which a successful vaccine has been developed...and (does) not cross infect humans, and can be safely studied in poultry. **Using *Eimeria* vaccine as a surrogate, most if not all problems with *Plasmodium* vaccines can be worked upon first and solved if possible, without using human volunteers**.

Importantly, this paragraph goes on to say that *Eimeria* vaccines can be used to develop an effective *Plasmodium* vaccine and to determine an effective regime for its administration, including the dosages and timing, specifically.

On pages 6-9, the RFA provides D2, Wallach and the following four references as evidence supporting that this information was part of the CGK: Blake et al., Frölich et al. 2014, Lim et al. and Gopalakrishnan et al.

…

Wallach, D2 and Gopalakrishnan et al. are all review articles which the MOPOP § 12.02.02c refers to in the group of established reference works that are relevant to identifying CGK. However, none of these references provide or refer to any examples where the response of a chicken to *Eimeria* parasites was used as a model to determine something as specific as the effective dosage or timing of a vaccine candidate or antimalarial treatment in humans. Likewise, Blake et al., Frölich et al. 2014 and Lim et al.—which are not review articles—provide no such examples.

Based on the record as it presently stands we do not agree that the above references support the contention that it was generally known and accepted without question by the bulk of those in the field that an *Eimeria* vaccine in a chicken model

can be used as an appropriate surrogate for determining the dosage and timing of a live *Plasmodium* vaccine that would be effective in humans.

To ascertain what was commonly and generally known about testing vaccine candidates in animal models we referred to the general guidelines set out by the World Health Organization's Expert Committee on Biological Standardization:

Annex 1, TRS No 924: Guidelines on clinical evaluation of vaccines: regulatory expectations (November 2004), Part A. Preclinical and laboratory evaluation of vaccines[10] (WHO guidelines)

When it comes to choosing an appropriate animal as a model for testing immunogenicity and protection, the guidelines state that the infection elicited by the microorganism should resemble the human infection and human immune response to the extent possible (page 53). Further, the guidelines state that the aim of animal and laboratory testing is to define the physical and biological characteristics of the same vaccine candidate that is intended for use in humans, including the indicators of safety and immunogenicity in an appropriate animal model (page 49). The guidelines also state that the efficacy data derived from such animal models can help in the selection of the doses, schedules and routes of administration to be evaluated in humans (pages 52-53). Our preliminary view is that this information in these international guidelines would have been known and accepted without question by the bulk of those engaged in the field of vaccine development.

To the extent that early testing in animal models plays a role in selecting the first dosages and schedules to test in humans, our preliminary view is that the skilled person would know that such studies would, at a minimum, test the same vaccine candidate, which in this case would be live *Plasmodium* parasites, not *Eimeria*. This is consistent with D3 that indicates prior testing of a live *Plasmodium* vaccine had been conducted in a rodent model where, unlike *Eimeria* in chickens, the liver and blood cells are infected in a manner similar to humans.

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[10] https://www.who.int/publications/m/item/guidelines-on-clinical-evaluation-of-vaccines-regulatory-expectations

> For these reasons, contrary to what is said in the application at para 32, our preliminary view is that the skilled person would not consider an *Eimeria* vaccine in a chicken model as an appropriate surrogate for investigating efficacy and dosing of a live *Plasmodium* vaccine in humans. As such, subject to any further comment from the Applicant, we have not included this as part of the CGK for our analysis.

[42] In the RPR letter, the Applicant did not contest or dispute our preliminary views that the six references from the RFA fail to support that it was CGK to use *Eimeria* as a model for determining the dosage and timing of a live *Plasmodium* vaccine in humans. Instead, the Applicant provided a new argument that the skilled person reading the *Eimeria* examples in the description through the lens of the CGK would interpret the results as evidence that, despite their differences, an *Eimeria* vaccine could be used as a model to develop a human *Plasmodium* vaccine: (pages 2-3, emphasis added)

> While knowledge of the life cycle of apicomplexan parasites is helpful in the design of experiments, **a critical component of the CGK is interpretation of experimental vaccination results**.
>
> …even though *Eimeria* have finite or self-limiting life cycles, Applicant wishes to emphasize that the immune responses of birds protected them from a lethal *Eimeria* challenge as shown in the **prior art** (see pages 9-11 and 20-22, particularly, paragraph [0079], of the present application) and the Examples (see, for example, Table 4, in the present application). So the finite nature of the *Eimeria* life cycle had no impact on vaccine efficacy because the immunized birds were able to stand up to a lethal challenge.…So regardless of whether replication is finite or infinite, both the *Plasmodium* examples in Roestenberg et al. (D3) and the *Eimeria* examples show that immunity is achieved. **Thus, according to the CGK**, what is important for a successful live vaccine is that an infective organism reaches the host and is able to replicate to allow it to induce immunity.
>
> …
>
> Thus, with respect to using a live *Eimeria* vaccine as a model for developing a human vaccine using live *Plasmodium* parasites, Applicant submits that the CGK set

> out above sufficiently supports the use of the live *Eimeria* vaccine as a model to develop a human vaccine using live *Plasmodium* parasites.

[43] We note that the above reference to prior art disclosed in the application concerning *Eimeria* is referring to commercial poultry vaccines against coccidiosis, including Immucox®. Even though this information is identified as prior art, our view is that it is reasonable that knowledge of the commercial live *Eimeria* vaccines that successfully protect against coccidiosis would have been CGK to the skilled person.

[44] With regard to the *Eimeria* examples disclosed in the application, however, our view is that the logic in the RPR letter is circular. Examples that are disclosed for the first time in the application cannot have been part of the CGK at the time the application was published, nor could they retroactively transform other information into CGK prior to the publication date.

[45] To the extent that the Applicant is arguing that the skilled person would interpret facts from the CGK, i.e., that successful live *Eimeria* and *Plasmodium* vaccines both exist, as evidence that one could be used as a model for the other, we do not agree. The CGK is generally a collection of objective facts and in our view any interpretations of those facts, or based on those facts, are more appropriately considered as part of the utility analysis. Further, that interpretation would not be consistent with the WHO guidelines on animal models provided in Annex 1.

[46] The RPR letter did not dispute that the WHO guidelines would have been CGK but it did express the view that we read those guidelines narrowly: (page 3, emphasis added)

> The PAB has referred to the WHO guidelines regarding appropriate animal models. The PAB have **interpreted the WHO guidelines in this regard to be narrowly limited to animal models with the same organism**. However, one skilled in the art would appreciate that efficacy of the claimed vaccine would be recognized based on the efficacy of a like vaccine in *Eimeria* since it goes through the same intermediate

stages as *Plasmodium*, and to achieve efficacy, the live organism just needs to be present in the vaccine as per the CGK.

[47] By our reading of the guidelines in Annex 1, the WHO recommends that the vaccine candidate should be the same or as close to the human vaccine as possible. The primary goal of preclinical (i.e., pre-human) testing of a vaccine product is to determine whether that vaccine is suitable for testing in humans (page 49). The guidelines also indicate that the disease and immune response that is elicited by a specific vaccine candidate in the animal should resemble the human disease and human immune response to the extent possible (pages 52-53). In that view, an alternative animal model of human *Plasmodium* infection that adheres to these guidelines, i.e., the rodent model discussed in D3, was already well known to the skilled person. For that reason, based on the CGK set out in the WHO guidelines, our view is that the skilled person would not reasonably consider testing an *Eimeria* vaccine in a chicken as being appropriate for investigating the efficacy or selecting the doses or dosing schedules of a human *Plasmodium* vaccine.

[48] For all of these reasons and the reasons provided in our PR letter, our view is that the skilled person would not have known nor accepted without question that testing an *Eimeria* vaccine in a chicken model was an appropriate surrogate for developing a human *Plasmodium* vaccine.

[49] Finally, in the RPR letter the Applicant provided evidence from the following review article Aly et al. supporting that it was known that live *Plasmodium* can amplify 10,000 fold during the mammalian liver stage of infection:

Aly A S I et al, “Malaria parasite development in the mosquito and infection of the mammalian host” (2009) 63 Annu Rev Microbiol 195-221

[50] This was introduced as part of the utility analysis but in our view it is appropriately considered here since facts and information supporting a sound prediction can only be considered if they were disclosed in the application or were part of the CGK: *Bell Helicopter* paras 152-153.

[51] Since Aly et al. is a review article and this information is discussed in the introduction section of the article as part of the general background information we agree and accept that this information was part of the skilled person's CGK.

Meaning of terms

[52] We said the following on page 15 of our PR letter in relation to the meaning of "is used" in dependent claims 5 and 6:

> Claims 5 and 6 are dependent claims adding the limitation that the vaccine "is used" on a third consecutive day:
>
> 5. The use of claim 1 or claim 4 wherein the live low dose malaria vaccine is used on a third consecutive day.
>
> 6. The live low dose malaria vaccine of claim 2 or claim 3 wherein the live low dose malaria vaccine is used on a third consecutive day.
>
> In view of the exclusion of methods of medical treatment as patentable subject-matter, it is important to carefully consider the wording of claims for medical uses, including products for medical use, to ascertain whether the claim covers the use or equates to a method. Neither of the above preambles directs the claim to a method. However, our preliminary view is that the skilled person reading the claims in the context of the specification as whole would interpret "is used on a third consecutive day" as an active method step that is to be performed.

[53] In the RPR letter, the Applicant did not comment on, contest or dispute our preliminary view that the skilled person would interpret "is used on a third consecutive day" as an active method step that is to be performed. Instead, the Applicant proposed cancelling claims 5 and 6 outright and using wording in proposed claims 1 to 4 that the Applicant submits would not encompass an active step.

[54] For the same reasons provided above, our view is that the skilled person would interpret "is used on a third consecutive day" as an active method step that is to be performed.

Essential elements

[55] In our PR letter we expressed our preliminary view that all of the elements set out in the claims on file are essential (page 16):

> As mentioned above, we consider that all of the elements set out in a claim are presumed essential unless it is established otherwise or such presumption is contrary to the claim language. In our view, the skilled person reading claims 1-14 in the context of the specification as a whole and the CGK would understand that there is no use of language in the claims indicating that any of the elements are optional, preferred or were otherwise intended as being non-essential. Our preliminary view is therefore that all of the elements of claims 1-14 are essential.

[56] The Applicant made no submissions in respect of this construction in the RPR letter. We proceed on the basis of the essential elements as set out in our PR letter.

The utility of claims 1-14 was not established by demonstration or sound prediction as of the filing date

[57] As stated above in the legal principles section, the first step in the test for utility is to identify the subject-matter of the invention as claimed in the patent application and the second step is to ask whether that subject-matter is useful—if it is capable of a practical purpose, i.e. an actual result: *AstraZeneca*, at para 54.

[58] We said the following in our PR letter on pages 17-18:

> This first step was not formally addressed as such in the FA and RFA, although the FA appears to consider this in terms of the ability of the claimed subject-matter to prevent malaria (page 3):
>
> > The claims are directed to the use of a live low dose malaria vaccine consisting of *Plasmodium* infected mosquitoes wherein the target population is exposed to the mosquitoes and receive at least 5 mosquito bites on each of two or three consecutive days for the prevention of malaria.

> By contrast…the RFA associates the utility with the ability of the claimed subject-matter to induce an immune response.
>
> Providing the full protective immunity that would be required to prevent malaria is clearly a higher threshold than simply inducing an immune response. However, the Applicant has explicitly defined this higher threshold as the practical purpose of using the claimed vaccine regimen by asserting "for preventing malaria" as an essential element of the claimed subject-matter in all claims 1-14 on file. As such our preliminary view is that preventing malaria is the utility that had to be established as of the filing date.
>
> The second step in the analysis is to determine whether this was established by demonstration or sound prediction. The Applicant submits…that the claimed invention is clearly based on a sound prediction.

[59] The Applicant did not dispute our preliminary view that "preventing malaria" is the utility that had to be established for the claims on file. However, the Applicant did infer from our statements that our view is that the method must achieve full protective immunity in order to prevent malaria and comply with section 2 of the *Patent Act* (page 3 of the RPR letter):

> The PAB is of the view that "*for preventing malaria*" is an essential element of the claim and that the method must achieve full protective immunity in order to prevent malaria and comply with section 2.

[60] To clarify, our view in the PR letter is not that the claimed vaccine regimen would have to be shown or predicted to prevent malaria in 100% of subjects in order to satisfy the utility requirement. We note that our comments in the PR letter were intended to contrast "inducing an immune response" with the high bar of full or 100% protective immunity (from the description's discussion of the *Eimeria* experiments on pages 36-37) as representing opposite ends of a spectrum.

[61] Since preventing malaria is expressly asserted as being part of the claimed subject-matter and is an essential element of each of claims 1-14 our conclusion is that this is the utility that had to be established for claims 1-14.

[62] In the RPR letter the Applicant did not provide any evidence of demonstration or contest our approach in considering whether the utility had been established by sound prediction and so we adopt this approach for step 2.

Factual basis

[63] On pages 18-20 in our PR letter we addressed a number of statements from the Applicant's description and the RFA in order to clarify what information the skilled person would consider as being relevant and factual, ultimately expressing our preliminary view that the following facts from the description and CGK would form the factual basis (pages 20-21):

> live vaccination using mosquitoes infected with *P. falciparum* is well-known; a vaccine regimen of three doses of 12-15 bites administered at one month intervals (with chloroquine) provides full protective immunity in humans with some level of immunity reached after the first and second parasitemic episodes; that a useful live vaccine would, at a minimum, need to reliably induce infection; and that a human subject needs to be exposed to at least 5 bites from mosquitoes infected with *P. falciparum* to achieve a 100% infection rate.

[64] The Applicant made no submissions in respect of this list forming the factual basis. We proceed on the basis of the factual basis set out in our PR letter.

Line of reasoning

[65] The dosage regimen in the independent claims is modified in three main ways compared to the dosage regimen of the live *Plasmodium* vaccine used in humans in D3: the number of doses is changed from three to two; the dosing interval is changed from one month between doses to one day between doses; and the dose amount is changed from 12-15 mosquito bites/dose to as few as only 5 bites/dose.

[66] In our PR letter we expressed our preliminary view that the information disclosed in D3, which was CGK, and the *Eimeria* examples disclosed in the application

would not support a sound line of reasoning from the factual basis for predicting that the claimed regimen would prevent malaria.

[67] In the RPR letter, the Applicant proposed amending the claims to change the number of doses from two to three in all of the independent claims on file and provided arguments in favour of the patentability of those proposed claims.

[68] Even though the arguments were provided for the proposed claims, our view is that they are equally pertinent to the claims on file since dependent claims 5 and 6 also define using three doses and so we consider those arguments here.

[69] On pages 21-22 of our PR letter, we expressed our preliminary view that there is no sound line of reasoning for extrapolating the efficacy in preventing malaria that was achieved for the D3 regimen to the claimed regimen:

> The RFA attributes the line of reasoning in the description to the *Eimeria* examples and to the references provided as evidence supporting that *Eimeria* was accepted by those in the art as an appropriate model for studying *Plasmodium* vaccines (i.e., the six references discussed above under CGK): pages 6-11, emphasis added
>
> > ii) The sound line of reasoning connects the factual basis to the utility of the claimed invention. In the present case, the Applicant notes at (para 32) of the description that *Eimeria* vaccines are an appropriate surrogate for studying *Plasmodium* vaccines. This fact is well known by those of skill in the art…
> >
> > (D3) has shown that *Plasmodium* infected mosquito bites are effective as vaccines when dosed repeatedly at monthly intervals (see Figure 2A). Figure 2A shows a progressively reduced incidence of burden of submicroscopic parasitemia – each of the three submicroscopic parasitemia episodes corresponding to one of the three vaccinations. Indeed, **this is the same pattern seen by the Applicant in the instant application (e.g. in Table 4): that immunity is induced after two apicomplexan parasite life cycles are completed in the host...**

> Further with respect to a sound line of reasoning, having provided ample evidence that *Eimeria* is accepted as an appropriate model for vaccine development in *Plasmodium*, the Applicant points to the specific Examples in the present application which show that the claimed method is effective in the *Eimeria* model system. The Examples demonstrate that a second dose of vaccine when given on consecutive days in coccidiosis will hasten the appearance of protective immunity.

We have already expressed our preliminary view that the references do not support that it was accepted as CGK that a live *Eimeria* vaccine in a chicken could be used as a surrogate or model to determine the dosage and timing of a live *Plasmodium* vaccine in humans.

There is an important distinction between testing a human vaccine candidate in an animal model that is designed to mimic human infection and experimenting with a multivalent commercial vaccine developed for veterinary use in its intended host where the infection does not mimic human infection. Unlike *P. falciparum* in humans, *Eimeria* in chickens infects different cells, only one type of cell, carries out all stages of its life cycle within one host and the infection is self-limiting. Our preliminary view is that there are too many variables to make any specific predictions from the *Eimeria* examples in relation to the effective dosing regimen of a human *Plasmodium* vaccine.

To the extent that the skilled person reading the description would consider the *Eimeria* examples, the above passages from the RFA indicate that immunity is induced after two *Eimeria* life cycles are completed (referring to Table 4). However, this is not supported by Table 4 in the description: the chicks in that experiment received three 100 µL doses of the Immucox® vaccine, not two (see the protocol at para 106 for Example 1).

Notably, that same dose and protocol was repeated for Treatment group 1 in Example 2 and obtained the same positive results, but Treatment group 2 did not achieve 100% protective immunity. That group received either one, two or three doses of 50 µL, which is said to be the standard dose amount for full protective

immunity when Immucox is administered in chicks once per cycle for two cycles. From this, the description draws the following conclusion (para 114):

> it appears that the therapeutically effective amount for achieving early protective immunity is twice the minimum amount for achieving full protective immunity where the exposure is once per cycle for two cycles.

In our view, if the skilled person were to draw any broad conclusions from these examples it would be that moving the doses of an effective vaccine regimen closer together requires an increase in the dosage in order to maintain protective immunity. However, the claimed regimens all use a dose as low as 5 bites which constitutes a decrease in the dosage compared to the effective vaccine regimen from the factual basis, not an increase. The vaccine regimen from D3 uses doses of 12-15 bites from *Plasmodium*-infected mosquitoes when administered monthly. Consequently, our preliminary view is that the skilled person would not consider this as providing a line of reasoning that would soundly connect the factual basis to the utility.

[70] In response, the Applicant made three main arguments in the RPR letter. The first main argument is that the skilled person reading the results of the *Eimeria* experiments through the lens of the CGK, which includes knowledge of successful live *Plasmodium* and *Eimeria* vaccines, would interpret them as showing that efficacy will be achieved as long as the live organism is present in the vaccine (pages 2-3):

> Whether replication numbers are finite like *Eimeria* or infinite like *Plasmodium*, they still go through the same intermediate stages. To achieve efficacy, the live infecting organism just needs to be present inside the vaccinee, as shown in D3 and as further evidenced in the Examples of the present application…So regardless of whether replication is finite or infinite, both the *Plasmodium* examples in Roestenberg et al. (D3) and the *Eimeria* examples show that immunity is achieved. Thus, according to the CGK, what is important for a successful live vaccine is that an infective organism reaches the host and is able to replicate to allow it to induce immunity…Both vaccines in D3 and the Examples in the present application are dependent on infection, both are apicomplexa, the host reaction is the same for both, and both showed protective immunity in their respective hosts...

> …one skilled in the art would appreciate that efficacy of the claimed vaccine would be recognized based on the efficacy of a like vaccine in *Eimeria* since it goes through the same intermediate stages as *Plasmodium*, and to achieve efficacy, the live organism just needs to be present in the vaccine as per the CGK.

[71] To the extent that the same "host reaction" is referring to both humans and chickens having developed protective immunity in response to inoculation with their respective parasites administered according to their respective dosage regimens, we agree. However, in our view the skilled person would not consider the mutual success of the D3 *Plasmodium* vaccine, the commercial *Eimeria* vaccines and the *Eimeria* examples as evidence that the presence of live infectious organisms is all that would be required to achieve efficacy or success in preventing malaria.

[72] We have accepted as fact that a vaccine would, at a minimum, need to be able to reliably cause infection. However, contrary to Applicant's statements, we do not agree that the skilled person would consider this as the sole factor that would dictate efficacy. As we explained in our PR letter, it was CGK that the protective response elicited by a vaccine can be affected by other factors such as the dosages, schedules and routes of administration that are used: Annex 1. The Applicant did not dispute or contest that this was well known to the skilled person in the RPR letter. This is consistent with Example 2 disclosed in the application which showed that when the conventional commercial regimen of Immucox was changed the efficacy was impacted (as discussed at para 114). For these reasons, our view is that the skilled person would not reasonably interpret the *Eimeria* examples and D3 as showing that a vaccine would be effective in preventing malaria as long as live *Plasmodium* organisms are present.

[73] The second main argument is that the Applicant disputed that there is no evidence of any experiments where immunization using 5 mosquito bites, at any dose interval, was effective in preventing malaria in humans (RPR letter, page 4):

> Epstein et al. describes a *Plasmodium* challenge/vaccine that consists of allowing a human to receive 5 bites from *Plasmodium* infected mosquitoes. Because the 5 bite challenge in Epstein et al. is a *live* vaccine/challenge, the *Plasmodium* organisms

> start to replicate inside the bitten mammalian host, following which the numbers of *Plasmodium* parasite multiply into thousands of organisms, causing infection and symptoms that are whole body and overwhelming. For example, in Table 2 at page 147 of Epstein et al., 100% of volunteers in the study had fatigue and headache which were whole body symptoms as a result of *Plasmodium* infection that had taken hold in 100% of the volunteers receiving 5 bites each.

[74] First, saying that Epstein et al. describes a *Plasmodium* “challenge/vaccine” implies that these terms are interchangeable. However, the skilled person having a background in immunology and vaccine development would know that the terms “vaccine” and “challenge” have different meanings and are not synonyms. Vaccine efficacy is generally evaluated by administering a challenge to both a test group (i.e., patients that previously received a vaccine) and a control group (e.g., patients that received a placebo) and comparing the results to determine if the vaccine reduced the odds of developing clinical disease in the test group: see the Glossary of Annex 1, Epstein et al. or D3 which were all part of the CGK. Further, Epstein et al. distinguishes between vaccines and challenges. The mosquito bite challenge was not the vaccine, the challenge was used to test the efficacy of a number of different vaccines and antimalaria drugs to see if they worked to prevent or treat malaria (see, for example, the abstract and opening first paragraph of page 145).

[75] With this understanding, the skilled person looking at Table 2 in Epstein et al. would recognize from the results that the DNA vaccine in question failed to prevent headache and fatigue symptoms in the test subjects following the 5 bite challenge. In that study only 31 of the 47 patients that received the 5 mosquito bite challenge had previously been immunized using the DNA vaccine; the other 16 patients were part of a control group and all of the subjects developed those symptoms.

[76] Epstein et al. concludes from the Table 5 results that 5 mosquito bites reliably provides an infectious dose of *P. falciparum* in the control subjects. Epstein et al. does not, however, disclose using 5 bites from a mosquito infected with intact *Plasmodium* sporozoites as a vaccine candidate (as opposed to a challenge).

Based on the record as it stands there is no evidence of any experiments where as few as 5 bites from *Plasmodium*-infected mosquitoes were used as a vaccine, given at any dosing interval, that was shown to be effective in preventing malaria following a challenge.

[77] The Applicant's third main argument is that the difference between using a smaller dose of as few as 5 bites instead of the 12-15 bites used in D3 would be mathematically insignificant for the purposes of causing infection and inducing immunity (RPR pages 4-5):

> With a live vaccine, due to 10,000 fold replication in the liver, and further infection in the subsequent pathogenic erythrocytic cycle, the number of *Plasmodium* organisms increases exponentially over time within the vaccinee, as the *Plasmodium* continues along its usual life cycle.
>
> Epstein et al. showed that 5 bites with *Plasmodium* infected mosquitoes was enough to infect humans 100% of the time (see Table 5 and compare columns labelled "Control volunteers with parasitemia/total (includes nonvaccine studies), no." and "Bites no.").
>
> Once infection is achieved, which it is with 5 bites of *Plasmodium* infected mosquitoes, the dose is amplified within the body for a live vaccine because the *Plasmodium* from those 5 bites are living and replicating, leading to a 10,000 fold amplification at the liver stage.
>
> While the 5 bites of Epstein et al. is about 2.5 to 3 fold smaller than the 12 to 15 bites in Roestenberg et al. (D3), the amplification of the live *Plasmodium* organisms within the body by 10,000 fold renders this 2 to 3 fold difference to be mathematically irrelevant for the purposes of causing infection and inducing immunity, where 5 bites and 12 to 15 bites (which the PAB agrees results in 100% protective immunity) is insignificant because both initiate the infection process 100% of the time, both lead to exponential replication, including 10,000 fold liver stage amplification, and so it is not possible for one such regimen to have utility (12 to 15 bite regimen) and for the other (5 bite regimen) to lack utility.

[78] As stated above we have accepted that it was CGK, in view of Applicant's submissions in the RPR letter, that live *Plasmodium* can amplify 10,000 fold during the mammalian liver state of infection and so this information is appropriately considered in terms of the line of reasoning.

[79] Even if we accepted that the skilled person would consider the difference between a dose of as few as 5 bites compared to 12-15 bites as mathematically insignificant in the present case, that is not the only change that is made to the D3 dosage regimen.

[80] D3 demonstrated efficacy when three doses of 12-15 bites each from *Plasmodium*-infected mosquitoes are administered with one month between doses. In that experiment after enough time passed to clear the body of infection and chloroquine (or only chloroquine in the case of the control group receiving placebo), the vaccine group and control group subjects were all challenged with bites from 5 infected mosquitoes. All 10 subjects in the vaccine group were protected against the malaria challenge and all 5 control subjects developed parasitemia, demonstrating that the vaccine, administered according to that dosage regimen, was effective and reduced the odds of developing clinical disease in the test group.

[81] The claimed dosage regimen modifies the D3 regimen so that the doses are given only a day apart (instead of monthly). Also, fewer doses are given and each dose could comprise fewer mosquito bites (as few as only 5). It is not clear that a difference in the dosing of this magnitude, when sporozoites from a total of 36-45 bites are amplified 10,000 fold (as compared to only 10 or 15 amplified by the same factor) would be considered irrelevant by the skilled person. Especially since the application teaches that moving the doses in the regimen closer together would likely require an increase over the standard effective dosage (at para 114, discussed above in our PR letter).

[82] As we have explained above and in our PR letter, the impact that these three changes would have on the efficacy that is achieved using the D3 regimen is unknown. The skilled person would not reasonably rely on the *Eimeria* examples

because they involve a different immunizing agent and were not carried out in an animal model that mimics human infection. No testing was done to evaluate the effect that these changes would have in an appropriate animal model, such as by testing a live *Plasmodium* vaccine in a rodent, and whether malaria would still be prevented. In our view, this leaves a gap or disconnect in the line of reasoning between the factual basis and a sound prediction that the claimed regimen would still prevent malaria in humans. For this reason, our view is that the skilled person would not consider the application as providing a solid teaching and *prima facie* reasonable inference that malaria would be prevented using this regimen.

[83] Consequently, our conclusion is that the utility of the claimed subject-matter was not established by a sound prediction as of the filing date and claims 1-14 on file do not comply with section 2 of the *Patent Act*.

Claims 1-14 are supported and enabled

[84] In our PR letter we expressed our preliminary view that claims 1-14 are supported and enabled by the description (PR letter, pages 23-25):

> On page 5, the FA contends that claims 1-14 are not “fully supported” by the description and so the description does not comply with section 84 (now section 60) of the *Patent Rules*. In sum, the FA explains that there is no substantive support because there is no evidence in the description that the claimed *Plasmodium* dosage regimen would work to effectively prevent malaria in humans. The examples and their results were not considered as supporting the claims because they relate to a dosage regimen using *Eimeria* for preventing coccidiosis in a chickens.
>
> The FA further explains that this lack of supporting evidence renders the description non-compliant with subsection 27(3) of the *Patent Act*, insofar as it relates to claims 1-14. Additionally, the FA contends that it would require undue experimentation for a skilled person to determine if the claimed dosage regimen would be effective for preventing malaria in a human or in a human target population.

On pages 12-13, the RFA disputes that claims 1-14 are not supported since all of the characteristics of the claims are set forth in the description using the same terms which, according to MOPOP §16.05, is all that is required. The Applicant further contends that the ground for rejection appears to relate to utility as opposed to claim support.

With respect to compliance with subsection 27(3) of the *Patent Act*, the RFA says the following at page 14:

> As established by common law, there is no requirement to provide specific examples to establish utility, and certainly not to comply with written description and enablement requirements. With respect to the undue experimentation allegation, in view of the teachings of D3, it is difficult to understand how it could be that one of skill must exercise undue experimentation to practise the claimed method

We agree with the RFA for the following reasons.

First, there is no language in section 60 of the *Patent Rules* or subsection 27(3) of the *Patent Act* that explicitly requires the disclosure of examples or experimental results supporting that the invention works.

Second, we agree that consistent with MOPOP §16.05 all the characteristics of the claimed embodiments of the invention are fully set forth in the description using the same or reasonably inferable terms and this is sufficient for compliance with section 60 of the *Patent Rules*. In our view, based on the facts in this case, claims 1-14 are fully supported for the purposes of section 60 of the *Patent Rules* by the teachings set out on pages 5, 5a, 6 and 12-17.

Third, with respect to enablement, we agree with the RFA that everything required to perform the claimed subject-matter is found in the description and D3, which was part of the CGK. We further agree that there would be no undue experimentation required from the skilled person to use *Plasmodium*-infected mosquitoes in the manner taught on each of two or three consecutive days and see if it works.

Subsection 27(3) of the *Patent Act* requires disclosure of the invention. According to the Supreme Court of Canada in *Teva*, subsection 27(3) of the *Patent Act* does not

require disclosure of the utility, the disclosure of examples or the disclosure of test results in the description in order to fulfill the requirements of sufficiency or enablement (*Teva* at para 40, emphasis added):

> Nothing in this passage suggests that utility is a disclosure requirement; all it says is that "the utility required for patentability (s.2) must, as of the priority date, either be demonstrated or be a sound prediction". Utility can be demonstrated by, for example, conducting tests, but this does not mean that there is a separate requirement for the disclosure of utility. In fact, there is no requirement whatsoever in s. 27(3) to disclose the utility of the invention: see, e.g., *Consolboard*, at p. 521, *per* Dickson J.: "I am further of the opinion that s. 36(1) [now s. 27(3)] does not impose upon a patentee the obligation of establishing the utility of the invention".

For these reasons, we are satisfied that the claims comply with section 60 of the *Patent Rules* and that the description, insofar as it relates to claims 1-14 on file, complies with subsection 27(3) of the *Patent Act*.

[85] The Applicant expressed its agreement with our preliminary views in the RPR letter.

[86] For the reasons set out above, our conclusion is that the claims comply with section 60 of the *Patent Rules* and that the description, insofar as it relates to claims 1-14 on file, complies with subsection 27(3) of the *Patent Act*.

Claims 5 and 6 comprise a method of medical treatment

[87] We said the following on page 25 of our PR letter:

> As stated above methods of medical treatment are not patentable subject-matter but medical uses may be permitted provided they do not comprise essential elements that include active medical steps that would equate to a method of medical treatment.

> We have already expressed our preliminary views above that the skilled person would purposively construe “is used on a third consecutive day” as an essential element of claims 5 and 6 and that this would be interpreted as an active method step that is to be performed. In contrast to claims passively expressing that a medicinal agent is “for use”, essential elements that comprise an active medical treatment step run afoul of the methods of medical treatment exclusion. Consequently, in view of the current wording of these claims, our preliminary view is that claims 5 and 6 equate to methods of medical treatment that are excluded from the definition of “invention” in section 2 of the *Patent Act*.

[88] The Applicant did not dispute or contest the above in the RPR letter. Instead, the Applicant proposed an amendment cancelling claims 5 and 6 to remove the active medical steps.

[89] For the reasons provided in our letter, our conclusion is that the wording of claims 5 and 6 on file equates the subject-matter to methods of medical treatment that are excluded from the definition of “invention” in section 2 of the *Patent Act*.

PROPOSED CLAIMS 1-21

[90] As mentioned above, the Applicant submitted a set of proposed claims 1-21 with the RPR letter.

[91] Proposed claims 1-4 are the same as independent claims 1-4 on file except that the vaccine is given on each of three consecutive days (instead of two). The proposed amendments would further cancel claims 5 and 6 and renumber claims 7-14 on file as claims 5-12. Proposed claims 13 and 14 are added and are the same as proposed claims 11 and 12, respectively, except that they limit the number of mosquito bites provided per dose to 5. New proposed claims 15-21 are further included. Proposed claims 15-20 are the same as claims 1-4, 13 and 14 on file, respectively, (i.e., reciting dosing on two consecutive days) but would replace “for preventing malaria” with “to induce an immune response”. Proposed claim 21 also corresponds to independent claim 4 on file but would provide three doses instead of two and would replace “for preventing malaria” with “to induce an immune response”.

[92] In our view, the skilled person and the CGK would be the same for these proposed claims.

[93] In our view, the skilled person reading the proposed claims in the context of one another and the description would understand that using the live low dose malaria vaccine according to the regimen defined in the independent proposed claims 15-18 and 21 would induce an immune response but would not necessarily prevent malaria in the manner defined in proposed claims 1-14.

[94] For the same reasons set out above for the claims on file, our view is that all of the claim elements would be regarded as essential elements by the skilled person.

Methods of medical treatment

[95] Since the proposed amendments would cancel claims 5 and 6 on file outright and since we agree that the remaining proposed claims avoid wording that encompasses an active method step, we agree that the proposed claims would address that issue.

Utility

[96] With respect to step 1 in the test for utility, all of the proposed claims 1-14 assert preventing malaria as part of the claimed subject-matter and this is an essential element in each of these claims. Consequently, this is considered as the utility that had to be established for these claims for the same reasons as claims 1-14 on file.

[97] Since proposed claims 1-14 would use the vaccine on three consecutive days instead of two, our view is that these claims would lack utility for the same reasons set out above for claims 5 and 6 on file. Our reasons for the claims on file already address using two and three doses and we concluded that all of the claims on file lack a sound prediction of utility.

[98] However, the proposed amendment to replace “for preventing malaria” with “to induce an immune response” in proposed claims 15-21 would change step 1 of the analysis for these claims. In our view, this change would render those claims compliant with section 2 of the *Patent Act*. It was well known from Epstein et al. that the sporozoites delivered from as few as 5 bites of *Plasmodium* parasites induce an infection. In our view, it would be implicit to the skilled person that the infection would induce an immune response in humans and further that the ability to induce an immune response is independent of the number and frequency of doses used. We are therefore satisfied that the utility of proposed claims 15-21 would have been established by a sound prediction as of the filing date.

[99] However, for the following reasons, our view is that the subject-matter of proposed claims 15-21 would have been obvious to the skilled person.

Obviousness

[100] The legal principles for obviousness are set out below.

[101] Section 28.3 of the *Patent Act* requires claimed subject matter to not be obvious:

> The subject-matter defined by a claim in an application for a patent in Canada must be subject-matter that would not have been obvious on the claim date to a person skilled in the art or science to which it pertains, having regard to
>
> (a) information disclosed before the one-year period immediately preceding the filing date or, if the claim date is before that period, before the claim date by the applicant, or by a person who obtained knowledge, directly or indirectly, from the applicant in such a manner that the information became available to the public in Canada or elsewhere; and
>
> (b) information disclosed before the claim date by a person not mentioned in paragraph (*a*) in such a manner that the information became available to the public in Canada or elsewhere.

[102] In *Apotex Inc v Sanofi-Synthelabo Canada Inc*, 2008 SCC 61 at para 67 [*Sanofi*] the Supreme Court of Canada stated that it is useful in an obviousness inquiry to follow the following four-step approach:

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

[103] With respect to step 1, we have already identified the skilled person and the relevant CGK of that person above. Although the CGK is considered as of the publication date of the application our view is that all of the information identified above was also CGK as of the claim date.

[104] With respect to step 2, our view is that, following a purposive and complete reading of the application, the skilled person would construe the inventive concepts of proposed claims 15-21 as being the same as the claims as construed.

[105] With respect to step 3, our view is that the closest prior art is D3 since it is also directed to using live intact *Plasmodium* parasites as a malaria vaccine. The main difference that is common to the inventive concepts of all of proposed claims 15-21 is that the doses are given one day apart instead of one month apart as in D3. A second difference that is specific to the inventive concepts of proposed claims 15-20 is that only two doses are used instead of three doses as in D3. This is not a difference for proposed claim 21.

[106] With respect to the dose used, proposed claims 15-21 all define using at least five *Plasmodium* infected mosquitoes without limiting the number of bites they would deliver except for proposed dependent claims 19 and 20 which each specify a lower limit of at least 5 mosquito bites delivered by those mosquitoes. Since no upper limit is defined, our view is that the skilled person would reasonably consider the range to encompass the 12-15 bite dose disclosed in D3 and so this is not a further difference.

[107] We note that the dosage regimen used in D3 was shown to prevent malaria in 100% of subjects whereas the inventive concepts of proposed claims 15-21 state the regimen is used to induce an immune response. However, in our view this does not constitute a further difference because it would be implicit to the skilled person reading D3 that the dosage regimen used induces an immune response. Also, Figure 2A of D3 shows that the level of parasitemia following the second dose is lower than it is after the first dose, which is evidence that the first dose induced an immune response.

[108] With respect to step 4, our view is that the skilled person would not associate any degree of invention with any of proposed claims 15-21. As explained above, the skilled person would know from D3 that it would only require one dose of 12-15 bites to induce an immune response. Even if a dose of as few as 5 bites were used, it was CGK that this dose was enough to cause infection and, as explained above, the skilled person would understand that one dose of 5 bites would be enough to induce an immune response and that using a second or third dose would be unnecessary for that purpose. In this view, it would have been obvious to the skilled person that using the dosage regimen in proposed claims 15-21, which involves additional doses on a second or third consecutive day, would induce an immune response.

[109] For at least those reasons, our view is that there is no inventive ingenuity associated with the subject-matter of proposed claims 15-21 and the claims would not comply with section 28.3 of the *Patent Act*.

[110] Since the subject-matter of proposed claims 1-14 would not comply with section 2 of the *Patent Act* and the subject-matter of proposed claims 15-21 would not comply with section 28.3 of the *Patent Act*, proposed claims 1-21 do not qualify as “necessary” amendments for the purposes of subsection 86(11) of the *Patent Rules*.

CONCLUSIONS

[111] We conclude that the claims on file lack utility and are therefore non-compliant with section 2 of the *Patent Act* and that claims 5 and 6 on file are further non-compliant because they are directed to subject-matter that is excluded from the definition of “invention” in section 2 of the *Patent Act*.

RECOMMENDATION OF THE BOARD

[112] In view of the above, we recommend that the application be refused on the grounds that:

- claims 1-14 on file lack utility and are therefore non-compliant with section 2 of the *Patent Act*; and
- claims 5 and 6 on file further contravene section 2 of *Patent Act* because they equate to excluded methods of medical treatment.

Cara Weir	Maria Mill	Christine Teixeira
Member	Member	Member

DECISION OF THE COMMISSIONER

[113] I concur with the conclusions and recommendation of the Board that the application be refused on the grounds that:

- claims 1-14 on file lack utility and are therefore non-compliant with section 2 of the *Patent Act*; and
- claims 5 and 6 on file further contravene section 2 of *Patent Act* because they equate to excluded methods of medical treatment.

[114] Therefore, in accordance with section 40 of the *Patent Act*, I refuse to grant a patent on this application. Under section 41 of the *Patent Act*, the Applicant has six months within which to appeal my decision to the Federal Court of Canada.

Konstantinos Georgaras

Commissioner of Patents

Dated at Gatineau, Quebec

This 18th day of July 2023