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3 October 2025

Opposition - Decision Issued

Davies Collison Cave Pty Ltd
Level 28
500 Bourke Street
MELBOURNE VIC 3000
Australia

Your reference	35598589/CZG/SXD
Application number	2019346134
Applicant name	Janssen Biotech, Inc.
Opponent	Samsung Bioepis AU Pty Ltd

Dear Sir/Madam,

Please find attached a copy of a Decision of a Delegate of the Commissioner of Patents.

This decision may be appealed to the Federal Court. You can obtain more information from the website – www.fedcourt.gov.au.

Yours sincerely,

Tatiana Garzon
Oppositions and Hearings
Phone: 02 62832455

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AUSTRALIAN PATENT OFFICE

Samsung Bioepis AU Pty Ltd v Janssen Biotech, Inc. **[2025] APO 32**

Patent Application:	2019346134
Title:	Safe and effective method of treating ulcerative colitis with anti-IL12/IL23 antibody
Patent Applicant:	Janssen Biotech, Inc.
Opponent:	Samsung Bioepis AU Pty Ltd
Delegate:	Dr A. Lim
Decision Date:	3 October 2025
Hearing Date:	18 December 2024 in Sydney Further submissions filed 7 February 2025 and 21 February 2025
Catchwords:	**PATENTS** – section 59 – opposition to the grant of a patent – lack of novelty in light of documents established – whether disclosure of the results of the Phase III clinical trials is necessary for anticipation – the concept of parametritis considered – lack of inventive step in light of cited documents considered together with common general knowledge established – lack of support not established – opposition succeeds – costs awarded against applicant – opportunity to amend
Representation:	Counsel for the applicant: Julian Cooke SC, Joseph Elks Patent attorney for the applicant: Davies Collison Cave Counsel for the opponent: Christian Dimitriadis SC, Clare Cunliffe Solicitor for the opponent: Maddocks

IP AUSTRALIA

AUSTRALIAN PATENT OFFICE

Patent Application:	2019346134
Title:	Safe and effective method of treating ulcerative colitis with anti-IL12/IL23 antibody
Patent Applicant:	Janssen Biotech, Inc.
Date of Decision:	3 October 2025

DECISION

The opposition is successful on the grounds of novelty and inventive step. All the claims of the opposed application lack novelty in view of the cited prior art. All the claims of the opposed application lack inventive step in light of cited prior art considered together with CGK.

The opponent has not established that any of the claims lack support from subject matter disclosed in the opposed application.

Janssen Biotech, Inc. is given two months from the date of this decision to propose amendments to overcome the deficiencies in the claims.

Costs according to Schedule 8 are awarded against Janssen Biotech, Inc..

REASONS FOR DECISION

Background

1. Patent application 2019346134 (the **opposed application**) was filed on 24 September 2019 under the provisions of the Patent Cooperation Treaty. The opposed application claims priority from three US provisional applications and the earliest filing date of these applications is 24 September 2018.[1]

2. The opposed application was examined and advertised accepted by the Commissioner on 12 January 2023. Samsung Bioepis AU Pty Ltd (the **opponent**) filed a notice of opposition on 12

[1] The three US provisional applications from which the opposed application, 2019346134, claims priority are US 62/735,501 having a filing date of 24 September 2018, US 62/769,818 having a filing date of 20 November 2018, and US 62/895,774 having a filing date of 04 September 2019.

April 2023 and filed a statement of grounds and particulars (**SGP**) on 12 July 2023. The opponent requested amendments to the SGP on 12 October 2023, the applicant was given an opportunity to provide comments but chose not to do so, and the requested SGP amendments were allowed.

3. Evidence in support (**EIS**) was filed by the opponent on 12 October 2023. Janssen Biotech, Inc. (the **applicant**) filed evidence in answer (**EIA**) on 15 January 2024, and a request to make voluntary amendments to the claims of the opposed application on 29 January 2024. Leave to amend the specification was granted and details of the request to amend were subsequently advertised on 28 March 2024 for opposition purposes. No opposition was filed regarding the applicant's amendments of 29 January 2024. The amendments were allowed, and allowance of the amendments was published on 20 June 2024. Consequently, the applicant's amendments of 29 January 2024 form part of the specification and the opposition proceeds in respect of the amended claims.

4. Evidence in reply (**EIR**) was filed by the opponent on 18 March 2024.

5. A hearing was scheduled for Wednesday 18 December 2024 in Sydney. In accordance with the Commissioner's direction in the hearing notice, the opponent and applicant both filed a written summary of submissions before the hearing on the 04 December 2024 (the **OS**) and 11 December 2024 (the **AS**), respectively. On 16 December 2024, the opponent filed further written submissions in reply to the applicant's written submissions (the **ORS)**. On 17 December 2024, the applicant wrote a letter to the Commissioner alleging that the opponent's written reply submissions "would result in **significant prejudice to the Applicant** if they were to be considered by the Hearing Officer without the Applicant being afforded an adequate opportunity to consider the submissions and respond in writing" (emphasis in original). The applicant requested that the Commissioner urgently issue a direction to defer the hearing and provide the applicant with at least five business days to respond to the ORS.

6. A delegate of the Commissioner responded to the applicant's letter on the same day and indicated that it was not necessary to vacate the hearing scheduled for 18 December 2024 to afford the applicant procedural fairness. The delegate noted that to the extent that the applicant considered it was unable to properly respond to the ORS, the Commissioner can provide the Applicant with a period after the hearing to file written submissions that address the ORS. The delegate suggested that the applicant raise the issue of post-hearing submissions at the hearing and indicate how much time it considers appropriate to file further submissions. The delegate also noted that this would ensure procedural fairness while allowing the hearing to proceed.

7. At the hearing the applicant requested until 07 February 2025 to file written submissions to address the ORS. In all the circumstances, including the time of year being close to the Christmas and New Year holidays, I considered this period reasonable. I also agreed to the opponent's request for an opportunity to respond to the applicant's post-hearing submissions and gave the opponent two weeks after the filing of the applicant's post-hearing submissions to respond. I confirmed the provision of post-hearing submissions in a letter dated 19 December 2024 and noted that any post-hearing submissions had to be strictly limited to addressing matters in the ORS.

8. On 07 February 2025, the applicant filed post-hearing reply submissions (the **APHS**) to the ORS. The opponent filed responsive submissions to the APHS on 21 February 2025 (the **OPHS**). I am

satisfied that the APHS have been limited to the ORS and the OPHS have been limited to the APHS.

The opposition

9. The grounds of opposition stated in the SGP are:
    - lack of novelty,
    - lack of inventive step, and
    - lack of support.

10. The evidence is summarised in the able below.

Evidence	Declarant	Exhibits	Date	Reference
In Support	Stephen James Rohl	SJR-1 to SJR-6	12 October 2023	**Rohl #1**
	Veysel Kayser	VK-1 to VK-4	12 October 2023	**Kayser**
	Paul Pavli	PP-1 to PP-11	12 October 2023	**Pavli #1**
In Answer	Matthew Aaron Ciorba	MAC-1 to MAC-8	14 January 2024	**Ciorba**
	John Kornak	JK-1 to JK-5	13 January 2024	**Kornak**
In Reply	Stephen James Rohl	SJR-7 to SJR-19	18 March 2024	**Rohl #2**
	Paul Pavli	PP-12 to PP-13	18 March 2024	**Pavli #2**

11. Since the opposed application was filed on 24 September 2019 this application is governed by the *Patents Act 1990* (the ***Act***) as amended by the *Intellectual Property Laws Amendment (Raising the Bar) Act 2012*. This includes subsection 60(3A) of the *Act* which states:

> *(3A) If the Commissioner is satisfied, on the balance of probabilities, that a ground of opposition to the grant of the standard patent exists, the Commissioner may refuse the application.*

12. The standard of proof that applies to the present opposition is the balance of probabilities, and the opponent carries the onus of proof.

The specification

13. The field of the invention relates to

> "methods of providing a clinically proven safe and clinically proven effective treatment of ulcerative colitis, particularly moderately to severely active ulcerative colitis in patients who have had an inadequate response to or are intolerant of a conventional or existing therapy by intravenous and/or subcutaneous administration of an anti-IL-12/IL-23p40 antibody."[2]

14. The specification as amended up to this point in time has 30 claims. Claims 1, 17, 29 and 30 are the independent claims. The claim set is reproduced in Annex A of this decision.

[2] The specification at page 1, lines 13-17.

Principles of construction

15. Before commencing to construe the specification, I note what Middleton J said in *Eli Lilly and Company Limited v Apotex Pty Ltd*:

> "It is well settled that the Court should, from the outset, approach the task of patent construction with a generous measure of common sense. The Court must place itself in the position of a person skilled in the relevant art, being the subject matter of the patent. From this perspective, the patent is to be read as a whole, in the context of the specification and in light of the prevailing common general knowledge and state of the relevant art at the priority date."[3]

The person skilled in the art (PSA)

16. It is well established that many of the issues in an opposition are answered by reference to the PSA:

> "He is the person to whom the patent is addressed and who must construe it. He is the person whose knowledge will determine whether a patent is novel. He is the person who will judge whether a patent is obvious."[4]

17. However, the PSA is an artificial construct that is used as a tool of analysis, and there is a danger in trying to identify them as an actual person or persons:

> "The notional person is not an avatar for expert witnesses whose testimony is accepted by the court. It is a pale shadow of a real person – a tool of analysis which guides the court in determining, by reference to expert and other evidence, whether an invention as claimed does not involve an inventive step."[5]

18. An understanding of the PSA is based on evidence from persons with knowledge of the art as to the things that they know and do, and what they understand to be commonly known and done. The qualifications of the expert witnesses, relevant to the present opposition, are summarised below. The opponent relies on the evidence of Professor Paul Pavli, Associate Professor Veysel Kayser, and Mr Stephen James Rohl. The applicant relies on the evidence of Professor Matthew Aaron Ciorba and Professor John Kornak.

19. Professor Pavli is a gastroenterologist with almost 40 years of experience.[6] He has worked in the field of gastroenterology since 1984 and has lectured on the pathophysiology, treatment and management of IBD for over 25 years.[7] Professor Pavli has undertaken research focusing on the clinical and basic scientific aspects of IBD, particularly on the causes of Crohn's disease (**CD**) and ulcerative colitis (**UC**), the role of inflammatory cells in these diseases, and treatments for these diseases.[8] Since 1999, Professor Pavli has been involved in a number of clinical trials including investigation of new therapeutic agents and existing therapeutic agents (approved for conditions other than CD and/or UC) in the treatment of CD and/or UC as part of multinational,

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[3] [2013] FCA 214 at [139]; 100 IPR 451.
[4] *Root Quality Pty Ltd v Root Control Technologies Pty Ltd* [2000] FCA 980 at [70]; 177 ALR 231.
[5] *AstraZeneca AB v Apotex Pty Ltd* [2015] HCA 30 at [23]; 89 ALJR 798.
[6] Pavli # 1 at [1].
[7] Pavli # 1 at [15], [26].
[8] Pavli # 1 at [27].

multicentre research programs, frequently as a principal investigator.[9] He has also acted as an independent evaluator of applications to register new medicines and new indications for the Therapeutic Goods Administration on several occasions between 2001 and 2004, and served on the Australian Drug Evaluation Committee between 2005 and 2022.[10]

20. Associate Professor Kayser is a pharmaceutical scientist with almost 20 years' experience, particularly in relation to development, formulation and stability of biologic medicines and vaccines. He is an Associate Professor at the University of Sydney.[11]

21. Mr Rohl is a solicitor for the opponent. His declarations deal with the cited prior art and particular matters the opponent considered relevant to the CGK.

22. Professor Ciorba is a gastroenterologist, Professor of Medicine, and Director of IBDs Research at Washington University in St Louis, Missouri, in the United States.[12] Professor Ciorba has been specialising in gastroenterology since 2004 and his clinical practice and research is primarily directed to advancing care for patients affected by CD, UC and colon cancer.[13] His research includes defining pathways and mechanism of intestinal inflammation and the transition to colon cancer.[14] Professor Ciorba has been a principal investigator in multiple clinical trials for CD and UC treatments.[15] He has been a member of numerous scientific panels including the Colitis Foundation of America and the American Gastroenterological Association (**AGA**).[16]

23. Professor Kornak is a biostatistician at the University of California, San Francisco, in the United States.[17] Professor Kornak gives evidence on the role of statistical analysis in clinical studies.

24. The opponent submitted that the role of statistical analysis in clinical studies is entirely irrelevant to the questions of novelty, inventive step and support.[18] In the present circumstances, I consider that the grounds of opposition can be addressed adequately by considering the disclosure in the (1) cited prior art, together where appropriate, with CGK, or (2) specification. Therefore, for this opposition I am of the view that evidence on the role of statistical analysis in clinical studies is not necessary.

25. The opponent also submitted that Professor Ciorba's evidence (1) reflects matters peculiar to the USA, not the CGK worldwide, and (2) addresses the wrong standard as he often substitutes a test for prediction for a test of expectation.[19]

26. The applicant submitted that Professor Pavli's evidence (1) is limited to the CGK in Australia only, and (2) regarding the hypothetical task he was given for the assessment of inventive step, is tainted by hindsight because of his involvement in the Phase III clinical trial for ustekinumab (known as the UNIFI clinical trial) and his off-label experience with ustekinumab.[20]

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[9] Pavli # 1 at [29]-[30]; Annexure PP-3 to Pavli # 1.
[10] Pavli # 1 at [46]-[47].
[11] Kayser at [1].
[12] Ciorba at [1], Part B; Annexure MAC-2 to Ciorba.
[13] Ciorba at [1], [12].
[14] Ciorba at [16].
[15] Ciorba at [18].
[16] Ciorba at [28].
[17] Kornak at [1].
[18] The OS at [12(b)].
[19] The OS at [12(a)]; the ORS at [6].
[20] The AS at [18], [199]; Annexure PP-3 to Pavli # 1.

27. I consider that Professor Pavli and Professor Ciorba emphasised the practices in their own jurisdiction but were aware of the CGK worldwide. I will consider the evidence of all declarants in the context of their experience and knowledge. The weighing and evaluating of the evidence are part of the normal work of a delegate of the Commissioner.

The background to the invention

28. The specification describes inflammatory bowel diseases (IBDs), which include ulcerative colitis (UC), as chronic relapsing disorders characterised by destructive inflammation and epithelial injury in the gastrointestinal (GI) tract.[21]

29. The etiology of UC is described as unknown but abnormal immune responses to contents in the gut, including intestinal microbes, are thought to drive disease in genetically predisposed individuals.[22]

30. The specification describes the involvement of the IL-12/IL-23 pathway in the pathogenesis of IBD to be well-established and that an important role for the IL-12/IL-23 pathway in intestinal inflammation has been elucidated in colitis.[23]

31. Biologic therapies that are currently approved for the treatment of UC are described to be either tumour necrosis factor (TNF) or integrin inhibitors. However, out of all the approved treatments, only vedolizumab has demonstrated efficacy in subjects who have had an inadequate response or are intolerant to anti-TNFs.[24] Furthermore, it has been observed that there are subjects receiving vedolizumab for the treatment of UC who show inadequate response and intolerance to their treatment.[25]

32. Biologic therapies that are currently approved for the treatment of UC are described to also demonstrate efficacy in CD.[26] The specification explains that multiple lines of evidence suggest that inflammatory bowel disease (UC and CD) is mediated by T helper 1 (**Th1**) or T helper 17 (**Th17**) cells with strong contribution from the proinflammatory cytokines, IL-12 and IL-23.[27]

33. The specification describes ustekinumab (STELARA®) to be a fully human monoclonal antibody to human IL-12/23p40 that prevents IL-12 and IL-23 bioactivity by inhibiting their interaction with the cell surface IL-12Rß1 receptor protein. Ustekinumab effectively neutralises IL-12 (Th1)- and IL-23 (Th17)-mediated cellular responses through this mechanism of action.[28] Ustekinumab is described as having received marketing approval in countries in North America, Europe, South America and the Asia-Pacific region, for the treatment of adults with moderately to severely active CD, moderate to severe plaque psoriasis, or active psoriatic arthritis, as well as for paediatric subjects (12 to 17 years old) with moderate to severe plaque psoriasis. The first approval for CD was received on 11 November 2016.[29]

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[21] The specification at page 1, lines 20-22.
[22] The specification at page 1, lines 27-29.
[23] The specification at page 2, lines 6-8.
[24] The specification at page 2, lines 24-27. I understand vedolizumab to be an integrin inhibitor.
[25] The specification at page 2, line 29 to page 3, line 1.
[26] The specification at page 3, lines 3-4.
[27] The specification at page 3, lines 5-7.
[28] The specification at page 3, lines 7-12.
[29] The specification at page 3, lines 12-17.

34. The specification explains that the efficacy and safety of intravenous ustekinumab therapy in CD have been evaluated in clinical studies.[30] Ustekinumab is reported to demonstrate clinically significant efficacy compared with placebo and was well tolerated with a favourable safety profile.[31]

Aim of the invention

35. The specification explains that there is a need in the art for improved methods of treating UC, particularly moderate to severely active UC in subjects who had previously failed or were intolerant of a biologic therapy or other conventional therapy, or subjects who had demonstrated corticosteroid dependence.[32]

36. The summary of the invention is described in similar terms of the field of the invention outlined above, this being:

> "clinically proven safe and clinically proven effective methods and compositions for treatment of moderately to severely active ulcerative colitis (UC), particularly in subjects who have had an inadequate response to or are intolerant of a conventional or existing therapy, by administration of an anti-IL-12/IL-23p40 antibody to subjects, thereby addressing a clear unmet medical need in this subject population."[33]

37. I infer that the aim of the invention is to provide an alternative method of treating UC, particularly in a subject who has had an inadequate response to, or is intolerant of, a conventional or existing therapy, by administration of an anti-IL-12/IL-23p40 antibody.

38. It is useful to note here that the specification uses the terms "anti-IL-12/IL-23p40 antibody", "IL-12/23p40 antibody", "anti-IL-12 antibody" and "anti-IL-23 antibody", interchangeably to refer to a monoclonal antibody (mAb) or antigen binding fragment thereof, that binds to the 40 kDa (p40) subunit shared by cytokines interleukin-12 and interleukin 23 (IL-12/23p40).[34] Ustekinumab is an embodiment of such a mAb.[35]

The invention as described in the specification

39. The specification uses some terms to describe various parts of an antibody that are understood by the skilled person. It is useful to provide an explanation of some of these terms here. Professor Ciorba provides a drawing of a typical structure of an antibody adapted from *Hansel et al* 2010 *Nature Reviews Drug Discovery 9*, 325-338).[36] I reproduce the drawing below.

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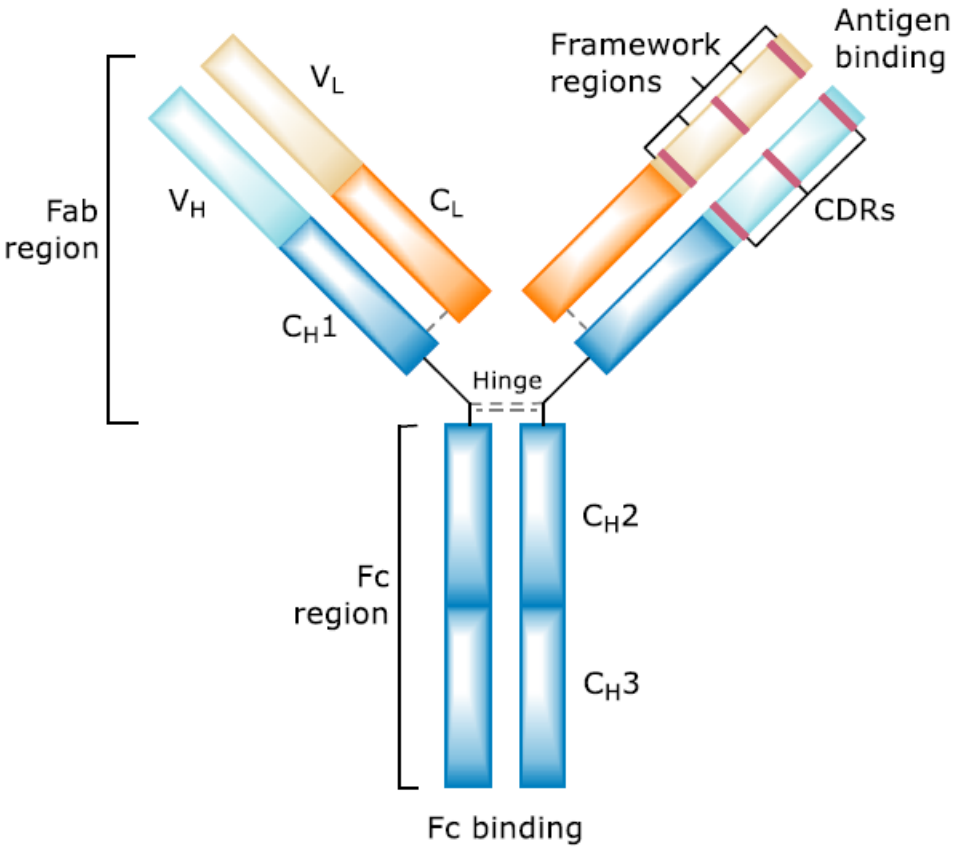
[30] The specification a page 3, lines 18-19.
[31] The specification at page 3, lines 27-28.
[32] The specification at page 4, lines 1-4.
[33] The specification at page 4, lines 9-13.
[34] The specification at page 10, lines 19-22.
[35] The specification at page 31, lines 16-18.
[36] Ciorba at [73].



40. Professor Ciorba explains that:

> "Broadly speaking, an antibody molecule is made up of four polypeptide chains; two heavy chains and two light chains (colored blue and orange respectively, in [the drawing above]). The heavy chains are partially bound together in a 'Y' shape, and each heavy chain is linked to a light chain by disulphide bonds.
>
> Each arm of the Y-shaped antibody structure is formed by the association of a light chain with the amino-terminal half of a heavy chain, to form the Fragment Antigen Binding (**Fab**) region that contains the antigen-binding site. The antigen binding site contains complementarity determining regions (**CDR**s), which are short stretches of amino acid sequences within the variable domains of the heavy chain and light chains (**VH** and **VL**, respectively), that come into contact with the antigen (i.e., a specific site on a target molecule). Generally speaking, the amino acid sequence of the CDRs informs the binding specificity and affinity of the antibody molecule. The stem of the Y-shaped antibody structure is the Fragment Crystallizable (**Fc**) region, formed by the constant regions of the heavy chains, and is responsible for antibody effector function, as the region interacts with Fc receptors and complement proteins. The Fc region is typically not important for targeting and neutralising soluble antigens, including soluble inflammatory cytokines. However, the Fc region can play a role in pharmacokinetics / bioavailability."[37] (bold font in original)

[37] Ciorba at [73]-[74].

41. The specification describes several aspects of the invention, and each aspect generally mirrors an independent claim in the claim set (as amended on 29 January 2024) of the present invention. A first aspect is a method of treating moderately to severely active UC in a subject in need thereof, comprising:

    - administering to the subject a pharmaceutical composition comprising an effective amount of anti-IL-12/IL-23p40 antibody,
      wherein
    - after treating with the antibody, the subject is a responder to treatment by at least one measure of response to treatment selected from a group consisting of seven efficacy criteria which are defined.[38]

42. The efficacy criteria are defined by reference to (a) various indices for measurement of disease activity including a Mayo Score, or a Mayo subscore, or (b) an Inflammatory Bowel Disease Questionnaire (IBDQ) score which is an assessment of disease-specific health-related quality of life.[39]

43. The Mayo score is described as an established, validated disease activity index for mild, moderate, and severe ulcerative colitis (UC) that is calculated as the sum of the four subscores of stool frequency, rectal bleeding, findings of endoscopy, and physicians' global assessment (PGA), and its value ranges from 0-12. A score of 3-5 indicates mildly active disease, a score of 6-10 indicates moderately active disease, and a score of 11-12 points indicates severe disease.[40]

44. The specification defines "clinical response" as a decrease from induction baseline in the Mayo score by ≥30% and ≥3 points, with either a decrease from baseline in the rectal bleeding subscore ≥1 or a rectal bleeding subscore of 0 or 1.[41]

45. A second aspect of the invention described is a method of treating moderately to severely active UC in a subject in need thereof, comprising:

    - (a) intravenously administering to the subject an anti-IL-12/IL-23p40 antibody in a first pharmaceutical composition at a dosage of about 6.0 mg/kg body weight of the subject or 130 mg, 260 mg, 390 mg or 520 mg per administration at week 0 of the treatment,
      and
    - (b) subcutaneously administering to the subject the anti-IL-12/IL-23p40 antibody in a second pharmaceutical composition at a dosage of 90 mg per administration at week 8 of the treatment,
      wherein
    - the subject is a responder to treatment by at least one measure of response to treatment selected from a group consisting of seven efficacy criteria which are defined,
      and wherein
    - the subject had previously failed or was intolerant of at least one therapy selected from a group consisting of five defined therapies (these being, an anti-TNF, vedolizumab,

[38] The specification at page 4, line 14 to page 4a, line 7. I note that two of the seven efficacy criteria were subsequently deleted from independent claim 1 in the amendments of 29 January 2024.
[39] The specification at page 4, line 25 to page 4a, line 7, and page 77, line 14.
[40] The specification at page 13, lines 19-24.
[41] The specification at page 14, lines 7-10.

corticosteroids, azathioprine (AZA), and 6 mercaptopurine (6 MP)), or the subject had demonstrated corticosteroid dependence.[42]

46. A third aspect of the invention described is a method of treating moderately to severely active UC in a subject in need thereof, comprising:

- (a) intravenously administering to the subject an anti-IL-12/IL-23p40 antibody in a first pharmaceutical composition at a dosage of about 6.0 mg/kg body weight of the subject or 130 mg, 260 mg, 390 mg or 520 mg per administration at week 0 of the treatment,
  and
- (b) subcutaneously administering to the subject the anti-IL-12/IL-23p40 antibody in a second pharmaceutical composition at a dosage of 90 mg per administration at week 8 of the treatment,
- followed by a maintenance therapy, wherein the maintenance therapy comprises subcutaneously administering to the subject the anti-IL-12/IL-23p40 antibody at a dosage of 90 mg per administration, once every 8 weeks or once every 12 weeks, wherein the maintenance therapy is provided for 44 weeks
  and
- after treating with the antibody, the subject is a responder to treatment by at least one measure of response to treatment selected from a group consisting of seven efficacy criteria which are defined.[43]

47. The anti-IL-12/IL-23p40 antibody of the first, second and third aspects of the invention is described to comprise a heavy chain variable region and a light chain variable region,

- the heavy chain variable region comprising a complementarity determining region heavy chain 1 (CDRH1) amino acid sequence of SEQ ID No:1, a CDRH2 amino acid of SEQ ID No:2, and a CDRH3 amino acid of SEQ ID No:3;
  and
- the light chain variable region comprising a complementarity determining region light chain 1 (CDRL1) amino acid sequence of SEQ ID No:4, a CDRL2 amino acid of SEQ ID No:5, and a CDRL3 amino acid of SEQ ID No:6.[44]

48. A fourth aspect of the invention described is a method of treating moderately to severely active UC in a subject in need thereof, comprising:

- (a) intravenously administering to the subject an anti-IL-12/IL-23p40 antibody comprising a heavy chain variable region of amino acid of SEQ ID No: 7 and a light chain variable region of amino acid SEQ ID No: 8 in a first pharmaceutical composition at a dosage of about 6.0 mg/kg body weight of the subject or 130 mg, 260 mg, 390 mg or 520 mg per administration at week 0 of the treatment,
  and

[42] The specification at page 4a, line 8 to page 4b, line 5. I note that two of the seven efficacy criteria were subsequently deleted from independent claim 17 in the amendments of 29 January 2024.
[43] The specification at page 4b, line 6 to page 4c, line 4. I note that two of the seven efficacy criteria were subsequently deleted from independent claim 29 in the amendments of 29 January 2024.
[44] The specification at page 4, lines 17-23, page 4a, lines 15-21, page 4b, lines 13-19. The amino acids of SEQ ID No: 1 to SEQ ID No: 6 are described in the sequence listings of the opposed application.

- (b) subcutaneously administering to the subject the anti-IL-12/IL-23p40 antibody in a second pharmaceutical composition at a dosage of 90 mg per administration at week 8 of the treatment,
- followed by a maintenance therapy, wherein the maintenance therapy comprises subcutaneously administering to the subject the anti-IL-12/IL-23p40 antibody at a dosage of 90 mg per administration, once every 8 weeks or once every 12 weeks, and
- after treating with the antibody, the subject is a responder to treatment by at least one measure of response to treatment selected from a group consisting of seven efficacy criteria which are defined.[45]

49. In some embodiments, the methods of the opposed application are described to comprise intravenously and/or subcutaneously administering to the subject a pharmaceutical composition comprising the anti-IL-12/IL-23p40 antibody ustekinumab, which comprises a heavy chain amino acid sequence of SEQ ID 10 and a light chain amino acid sequence of SEQ ID No:11.[46]

50. In some embodiments, the anti-IL-12/IL-23p40 antibody is in a pharmaceutical composition for intravenous administration comprising a solution comprising 10 mM L-histidine, 8.5% (w/v) sucrose, 0.04% (w/v) polysorbate 80, 0.4 mg/mL L-methionine, and 20 µg/mL EDTA disodium salt, dehydrate, at pH 6.0.[47]

51. In other embodiments, the anti-IL-12/IL-23p40 antibody is in a pharmaceutical composition for subcutaneous administration comprising a solution comprising 6.7 mM L-histidine, 7.6% (w/v) sucrose, 0.004% (w/v) polysorbate 80, at pH6.0.[48]

52. Examples 1 and 2 of the specification describe an induction study and a maintenance study, respectively, designed to assess the efficacy of ustekinumab in human subjects with moderately to severely active UC who demonstrated inadequate response to, or failure to tolerate, conventional (corticosteroids or 6-mercaptopurine (6-MP) or azathioprine (AZA)) or biologic therapy (TNF-antagonist and/or the integrin antagonist, vedolizumab).[49] Example 1 refers to a "Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Safety and Efficacy of ustekinumab Induction and Maintenance Therapy in Subjects with Moderately to Severely Active Ulcerative Colitis".[50] Professor Pavli and Professor Ciorba recognise Examples 1 and 2 of the specification as the induction study and the maintenance study, respectively, within a Phase III clinical trial for ustekinumab known as the UNIFI clinical trial.[51] The UNIFI clinical trial is described in a record that was published on the ClinicalTrials.gov

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[45] The specification at page 4c, lines 5-26. The amino acids of SEQ ID No: 7 and SEQ ID No: 8 are described in the sequence listings of the opposed application. I note that two of the seven efficacy criteria were subsequently deleted from independent claim 30 in the amendments of 29 January 2024.

[46] The specification at page 6, lines 3-7. The amino acids of SEQ ID No: 10 and SEQ ID No: 11 are described in the sequence listings of the opposed application.

[47] The specification at page 7, lines 18-20. As noted in the decision, specification uses the terms "anti-IL-12 antibody", "anti-IL-23 antibody", "anti-IL-12/IL-23p40 antibody" and "IL-12/23p40 antibody" interchangeably to refer to a monoclonal antibody (mAb) or antigen binding fragment thereof, that binds to the 40 kDa (p40) subunit shared by cytokines interleukin-12 and interleukin 23 (IL-12/23p40), see specification page 10, lines 19-22.

[48] The specification at page 7, lines 23-24. As noted in the decision, specification uses the terms "anti-IL-12 antibody", "anti-IL-23 antibody", "anti-IL-12/IL-23p40 antibody" and "IL-12/23p40 antibody" interchangeably to refer to a monoclonal antibody (mAb) or antigen binding fragment thereof, that binds to the 40 kDa (p40) subunit shared by cytokines interleukin-12 and interleukin 23 (IL-12/23p40), see specification page 10, lines 19-22.

[49] Example 1 begins on page 63 of the specification. Example 2 begins on page 75 of the specification.

[50] The specification at page 63, lines 12-14, page 64, lines 14-15.

[51] Pavli #1 at [259]; Ciorba at [237].

website, and this publication has been raised as a prior art citation (CTR 236) in the present opposition.[52] I will discuss CTR 236 in due course.

Example 1

53. In the induction study, subjects were randomised at week 0 to one of three treatment groups:
    a. Placebo
    b. "low-dose ustekinumab", which received a single 130 mg intravenous (IV) dose of ustekinumab; or
    c. "high-dose ustekinumab", which received a single weight-range based dose of approximately 6 mg/kg IV of ustekinumab, this being 260 mg for a body weight ≤55 kg, 390 mg for a body weight > 55 kg but ≤85 kg, and 520 mg for body weight >85 kg.[53]

54. All subjects were evaluated for clinical remission and clinical response at week 8.[54] Subjects who demonstrated no clinical response at week 8 received an additional IV or subcutaneous (SC) dose of ustekinumab.[55] Subjects who demonstrated a clinical response at week 8 or week 16 (following the additional dose) were eligible to enter the maintenance study, which is described to evaluate maintenance therapy using SC ustekinumab.[56]

55. Efficacy evaluations were collected throughout the clinical trial and the efficacy criteria for the induction study included:[57]

    a. clinical remission (global definition): Mayo score ≤2points, with no individual subscore >1;
    b. clinical remission (US definition): absolute stool number ≤3, rectal bleeding subscore of 0, and Mayo endoscopy subscore of 0 or 1;
    c. clinical response: a decrease from induction baseline in the Mayo score by ≥30% and ≥3 points, with either a decrease from baseline in the rectal bleeding subscore ≥1 or a rectal bleeding subscore of 0 or 1;
    d. endoscopic healing (i.e., improvement in the endoscopic appearance of the mucosa): Mayo endoscopy subscore of 0 or 1
    e. histological healing: based on the Geboes score and is defined as 0 to <5% neutrophils in the epithelium and no crypt destruction, erosion, ulcerations, or granulations;
    f. mucosal healing: both endoscopic healing and histologic healing

56. The efficacy results for the induction study are described as follows:

    "Clinical Remission at Week 8- Global Definition
    At Week 8, significantly greater proportions of subjects in the ~6 mg/kg and 130 mg groups achieved clinical remission (15.5% and 15.6%, respectively) compared with subjects in the placebo group (5.3%; p<0.001 for both comparisons; Table 1)."[58]

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[52] Pavli #1 at [259].
[53] The specification at page 64, line 15-17, page 65, lines 1-8.
[54] The specification at page 64, lines17-18.
[55] The dosages are described in the specification at page 65, lines 10-14. Subjects who were randomised to placebo at Week 0 received one weight-range based dose of approximately 6 mg/kg IV of ustekinumab +placebo SC, to maintain the blind, at Week 8. Subjects who were randomised to ustekinumab at Week 0 received one dose of 90 mg SC of ustekinumab + placebo IV, to maintain the blind, at Week 8.
[56] The specification at page 64, lines 18-29.
[57] The specification at page 66, line 24 to page 67, line 8.
[58] The specification at page 69, lines 20-24.

"Clinical Remission at Week 8- US Definition
At Week 8, significantly greater proportions of subjects in the ~6 mg/kg and 130 mg groups achieved clinical remission (18.9% and 16.6%, respectively) compared with subjects in the placebo group (6.3%; p<0.001 for both comparisons; Table 2)."[59]

"Clinical Response at Week 8
At Week 8, significantly greater proportions of subjects in the ~6 mg/kg and 130 mg groups achieved clinical response (61.8% and 51.3%, respectively) compared with subjects in the placebo group (31.3%; p<0.001 for both comparisons; Table 4)."[60]

"Endoscopic Healing at Week 8
At Week 8, significantly greater proportions of subjects in the ~6 mg/kg and 130 mg groups achieved endoscopic healing (27.0% and 26.3%, respectively) compared with subjects in the placebo group (13.8%; p<0.001 for both comparisons; Table 3)."[61]

"Histologic Healing at Week 8
Histologic healing was defined as 0 to <5% neutrophils in epithelium and no crypt destruction, erosions, ulcerations, or granulations. At Week 8, significantly greater proportions of subjects in the ~6 mg/kg and 130 mg groups achieved histologic healing (35.6% and 37.9%, respectively) compared with subjects in the placebo group (21.9%; p<0.001 for both comparisons)."[62]

57. The specification reports that median IBDQ scores were similar across all treatment groups at baseline, and

> "[a]t Week 8, the median improvements from baseline in the IBDQ scores were significantly greater in the ~6 mg/kg and 130 mg groups (31.0 and 31.5, respectively) compared with the placebo group (10.0; p<0.001 for both comparisons)."[63]

58. The specification also describes other efficacy criteria and reports the results for these other criteria.[64] Additionally, the results for the safety, pharmacokinetics and immunogenicity of administering ustekinumab intravenously are also reported.[65]

Example 2

59. Example 2 is a "[m]aintenance Study of ustekinumab in the treatment of ulcerative colitis in humans"[66]. The specification describes the "primary" population in the maintenance study as subjects who were in clinical response to IV Ustekinumab following the induction study, specifically:

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[59] The specification at page 70, lines 3-6.
[60] The specification at page 71, lines 4-6.
[61] The specification at page 70, lines 11-14.
[62] The specification at page 72, lines 15-19.
[63] The specification at page 71, line 11 to page 72, line 2. While the specification does not explain the reference point for "at baseline", the opponent's interpretation that this is Week 0 (see OS at [34]) seems reasonable in the context of the efficacy evaluation being made for changes to IBDQ scores.
[64] The specification at page 67, lines 9-22, page 72, lines 3 to page75, line 7.
[65] The specification at page 67, line 24 to page 69, line 18.
[66] The specification at page 75, lines 9-10.

a) Subjects who received 130 mg or ~6 mg/kg IV ustekinumab at induction week 0 and were in clinical response at induction week 8; and
b) Subjects who received placebo at induction week 0, were not in clinical response at induction week 8 but were in clinical response at induction week 16 after receiving ~6 mg/kg IV ustekinumab at induction week 8.[67]

60. The subjects were randomised at maintenance week 0 to receive ustekinumab 90 mg SC every 8 weeks (q8w), ustekinumab 90 mg SC every 12 weeks (q12w), or placebo SC.[68]

61. The specification describes the primary endpoint for the maintenance study to be clinical remission at week 44.[69] I understand the time for the primary endpoint to be maintenance week 44 of the study of Example 2 and diagrammatically represented in Figure 1 of the specification as "Overall Exposure" Week 52. In other words, the primary endpoint for the maintenance study of Example 2 is 52 weeks from induction week 0 as the period for the induction study was 8 weeks.

62. The definition of clinical remission (and the testing procedure) in the US is different to that outside the US. Two definitions of clinical remissions were applied to all subjects in the efficacy evaluation for the primary endpoint to accommodate the differences, these being:[70]

- The global definition stated as a Mayo score ≤2 points, with no individual subscore >1; and
- The US definition stated as an absolute stool number ≤3, a Mayo score rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1.

63. The efficacy results for clinical remission are described as follows:[71]

- Global definition: At week 44, the proportions of subjects in clinical remission were significantly greater in the ustekinumab q8w group and ustekinumab q12w group (43.8% and 38.4%, respectively) compared with subjects in the placebo group (24.0%; $p<0.001$ and $p=0.002$, respectively).
- US definition: At week 44, the proportions of subjects in clinical remission were significantly greater in the ustekinumab q8w group and ustekinumab q12w group (42.6% and 39.5%, respectively) compared with subjects in the placebo group (24.6%; $p<0.001$ and $p=0.002$, respectively).

64. Additionally, the specification reports:[72]

> "[a]pplying both global and US-specific definitions of clinical remission, the proportions of subjects achieving corticosteroid-free remission for at least 90 days prior to Week 44 was significantly greater ($p<0.01$) in the ustekinumab q8w and q12w groups compared with that in the placebo group. Furthermore, among subjects receiving corticosteroids at maintenance baseline, significantly greater proportions of subjects ($p<0.05$) were in clinical remission and not receiving concomitant corticosteroids for at least 90 days prior

[67] The specification at page 75, lines 9-21.
[68] The specification at page 75, lines 22-23.
[69] The specification at page 77, line 23.
[70] The specification at page 77, line 23 to page 78, line 2.
[71] The specification at page 80, lines 21-28.
[72] The specification at page 82, lines 4-11.

> to Week 44 in the ustekinumab q8w and q12w groups compared with those in the placebo group."

65. The efficacy results are also described for other efficacy criteria including maintaining clinical response, achieving endoscopic healing, achieving histologic healing and achieving mucosal healing.[73] Additionally, the results for the safety, pharmacokinetics and immunogenicity of administering ustekinumab subcutaneously are also reported.[74]

66. The specification states that the ustekinumab maintenance study provided evidence that the two dose regimens of administering 90 mg ustekinumab SC, q8w or q12w, were both effective in adult subjects with moderately to severely active UC who had responded to a single IV ustekinumab induction dose.[75] Additionally, the safety and efficacy data from the maintenance study support a "positive benefit/risk profile for ustekinumab SC maintenance therapy."[76]

67. The specification observes that STELARA® (ustekinumab) for the treatment of UC was approved in Europe as of 04 September 2019.[77]. Annex 1 of the opposed application reproduces the approved label (this being, the summary of product characteristics) for 130 mg (IV) STELARA®, and 45 mg or 90 mg (SC) STELARA®.[78]

The invention as claimed

68. The correct approach to the construction of claims was discussed by Bennett J in *H Lundbeck A/S v Alphapharm Pty Ltd.* ***(Lundbeck)****:*

> "the words in a claim should be read through the eyes of the skilled addressee in the context in which they appear … while the claims define the monopoly claimed in the words of the patentee's choosing, the specification should be read as a whole … it is not permissible to read into a claim an additional integer or limitation to vary or qualify the claim by reference to the body of the specification … terms in the claim which are unclear may be defined or clarified by reference to the body of the specification"[79]

Claim 1

69. It is convenient to parse claim 1, the first independent claims of the opposed application as follows:

    a) A method of treating moderately to severely active ulcerative colitis (UC) in a subject in need thereof, comprising

    b) administering to the subject a pharmaceutical composition comprising an effective amount of an anti-IL-12/IL-23p40 antibody,

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[73] The specification at page 81, line 7 to page 82, line 4.
[74] The specification at page 84, line 20 to page 88.
[75] The specification at page 88, lines 9-12.
[76] The specification at page 88, lines 22-23.
[77] The specification at page 89, lines 1-2.
[78] The specification reproduces the summary of product characteristics for 130mg (IV) STELARA®, at at pages 90-112, and that for 45 mg or 90 mg (SC) STELARA® at pages 113-148.
[79] [2009] FCAFC 70 at [118]-[120]; 81 IPR 228.

c) wherein the antibody comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region comprising: a complementarity determining region heavy chain 1 (CDRH1) amino acid sequence of SEQ ID NO:1; a CDRH2 amino acid sequence of SEQ ID NO:2; and a CDRH3 amino acid sequence of SEQ ID NO:3; and the light chain variable region comprising: a complementarity determining region light chain 1 (CDRL1) amino acid sequence of SEQ ID NO:4; a CDRL2 amino acid sequence of SEQ ID NO:5; and a CDRL3 amino acid sequence of SEQ ID NO:6,

d) wherein after treating with the antibody, the subject is a responder to treatment by at least one measure of response to treatment

e) selected from the group consisting of: (i) clinical remission based on at least one of the global definition of clinical remission with Mayo score ≤ 2 points with no individual subscore > 1 and the US definition of clinical remission with absolute stool number ≤ 3, rectal bleeding subscore of 0 and Mayo endoscopy subscore of 0 or 1, (ii) endoscopic healing with a Mayo endoscopy subscore of 0 or 1, (iii) clinical response based on the Mayo endoscopy subscore, (iv) mucosal healing, and (v) clinical response as determined by a decrease from baseline in the Mayo score by ≥30% and ≥3 points and a decrease from baseline in the rectal bleeding subscore ≥1 points or a rectal bleeding subscore of 0 or 1.

70. I will now consider the meaning of several terms of claim 1.

A method of treating moderately to severely active ulcerative colitis (UC) in a subject in need thereof

71. The applicant submitted that:

> "the Specification is clearly directed to 'clinically proven safe' and 'clinically proven effective' methods of treating moderately to severely active UC. These terms, and the term 'clinically proven', are defined in the Specification...As Prof. Ciorba explains, upon reading the Specification, it is apparent that:
>
> > … **to 'treat' a condition with a drug requires administering a drug that is known at that time to be capable of treating that condition in the relevant patient population**. A drug is only known to be capable of treating a condition if both its safety and efficacy have been established by Phase III clinical trial results ([except] where there is real world data collected from a large number of patients over a prolonged period of time that establishes safety and efficacy of that drug). [emphasis added]"[80]

72. The opponent submitted that the applicant's position is founded on:

> "the novel proposition that, in the context of the Application, 'treating' moderately to severely active UC involves administering a drug that is 'known' at the time of treatment to be safe and effective in a patient with moderately to severely active UC in the sense that the treatment had been the subject of a successful Phase III clinical trial.

[80] The AS at [72] which refers to Ciorba at [230].

> Unsurprisingly, that proposition does not reflect any definition of 'treating' which is incorporated into the Application. Nor does it reflect the plain and ordinary English meaning of the term 'treating' and normal use or understanding by any of the experts of the term. Further, the proposition is inconsistent with established case law in this area concerning methods of treatment, which demonstrates that the disclosure of something much less than the results of a Phase III clinical trial can anticipate: e.g., even a clinical protocol, or hypothesis, without any results or proof: see ***Mylan*** *Health Pty Ltd v Sun Pharma ANZ Pty Ltd* (2020) 279 FCR 354 at [104]-[111], especially [104]-[106]. Similar attempts to support the novelty or inventiveness of claimed methods of treatment based on an artificially elevated construction of 'treatment' have failed in other cases: see e.g. ***Astellas*** *Pharma Inc v Aragon Pharmaceuticals Inc* [2022] APO 36 at [49]-[146]"[81]

73. The applicant also submitted that based on a consideration of the Delegate in *Astellas Pharma Inc. v Aragon Pharmaceuticals, Inc.* (***Astellas***) a claim to a method of treatment should be understood as referring only to use in a population as distinct from one or more individual acts of treatment.[82]

74. At the oral hearing, the opponent submitted that such a construction would lead to an odd scenario where a claim to a method of treating a condition in a subject could not be considered an improvement unless there was improvement in subjects in a whole population. The opponent also observed that the claims in the present case are directed to a method of treating a condition *in a subject*. Additionally, the opponent submitted that a consideration based on the understanding in *Astellas* would be inconsistent with authorities and noted the finding of Nicholas J in *Apotex Pty Ltd v Warner-Lambert Company LLC (No 2) (**Warner-Lambert**)* who stated that "a claim will be infringed if a person administers a therapeutically effective amount of the relevant compound to a patient in need of treatment… for the purpose of providing such treatment even though the treatment may not be effective in that patient."[83]

75. The opponent also submitted that the fact that claims are to methods of treatment does not mean that the claimed responses must be achieved in every case and noted that Professor Pavli and Professor Ciorba agreed, as a matter of fact, that not all patients will respond to a particular treatment. [84] Furthermore, the opponent observed the results of the studies described in the present application (which are the UNIFI Phase III clinical trials) demonstrate this fact.[85]

76. While I understand I am to construe the claims in the context of the specification as a whole, it is "not legitimate to narrow or expand the boundaries of monopoly as fixed by the words of a claim by adding to those words glosses drawn from other parts of the specification."[86] The specification does describe examples of studies within a Phase III clinical trial to assess the efficacy of ustekinumab in human subjects with moderately to severely active UC. However, the words of claim 1 do not limit the method (a) to a treatment method that has already been clinically proven to be safe and effective, or (b) to a treatment method that is performed on any patient population. I would be impermissibly importing the requirements that the method be clinically proven on a patient population–in other words adding a gloss–if I were to adopt the applicant's construction of "treat".

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[81] The OS at [9].
[82] [2022] APO 36 at [103], [105].
[83] [2016] FCA 1238; 122 IPR 17 at [129]-[131].
[84] The OS at [47], citing Pavli #1 at 118(a) and Ciorba at [121].
[85] Ibid.
[86] *Jupiters Ltd v Neurizons Pty Ltd* [2005] FCAFC 90 at [67]; 65 IPR 86.

77. The Macquarie Dictionary defines "treat" as "to deal with (a disease, patient, etc) in order to relieve or cure".[87] Therefore, I interpret the plain meaning of the phrase "[a] method of treating moderately to severely active ulcerative colitis (UC) in a subject in need thereof" as indicating a method that is used with *an intended purpose to relieve or cure* a patient with moderately to severely active UC.

78. I also interpret the method of treatment defined in claim 1 to mean the treatment of one or more individuals suffering from moderately to severely active UC and is not limited to a subject population.

administering to the subject a pharmaceutical composition comprising an effective amount of an anti-IL-12/IL-23p40 antibody

79. I consider the PSA reading the specification would interpret this phrase to mean a subject is administered a pharmaceutical composition with a monoclonal antibody or antigen binding fragment that binds to the 40 kDa (p40) subunit shared by cytokines interleukin-12 and interleukin 23 (IL-12/23p40).[88] This antibody includes ustekinumab which was originally marketed by the applicant as Stelara®.[89] From a plain meaning of the words, an "effective amount" of antibody is an amount that is intended to effectively treat moderately to severely active UC.

wherein the antibody comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region comprising: a complementary determining region heavy chain 1 (CDRH1) amino acid sequence of SEQ ID NO:1; a CDRH2…of SEQ ID NO:2; and a CDRH3…of SEQ ID NO:3; and the light chain variable region comprising: a complementary determining region light chain 1 (CDRL1) amino acid sequence of SEQ ID NO:4; a CDRL2…of SEQ ID NO:5; and a CDRL3…of SEQ ID NO:6

80. I consider the PSA would understand the antibody of claim 1 to have a heavy chain variable region and a light chain variable region with the amino acid sequences as defined in the claim and with reference to the specification and sequence listing of the opposed application.

81. Professor Pavli observed that:

(a) the amino acid sequences of SEQ ID NO:1 to No:3 (heavy chain CDRs) are present in SEQ ID NO:7 (heavy chain variable region), and the amino acid sequence of SEQ ID NO:7 is present in SEQ ID NO:10 (heavy chain);

(b) the amino acid sequences of SEQ ID NO:4 to NO:6 (light chain CDRs) are present in SEQ ID NO:8 (light chain variable region), and the amino acid sequence of SEQ ID NO:8 is present in SEQ ID NO:11 (light chain);[90] and

[87] The Macquarie Dictionary Online, www.macquariedictionary.com.au, accessed 05 March 2025.
[88] The specification at page 10, lines 19-22.
[89] The specification at page 31, lines 16-18; Pavli #1 at [112], [280].
[90] Pavli #1 at [282].

(c) ustekinumab comprises a heavy chain having the amino acid sequence of SEQ ID NO:10 and a light chain having an amino acid sequence of SEQ ID NO:11.[91]

82. Professor Pavli stated that he understands claim 1 to refer to an antibody having the same CDRs as ustekinumab and includes ustekinumab itself. Additionally, Professor Pavli understands the antibody of claim 1 includes an antibody with the same variable regions as ustekinumab but with different constant regions to ustekinumab. However, he stated that he was not aware that any such antibody had been developed before 24 September 2018 nor to the day he made his statement on 12 October 2023.[92]

83. Professor Ciorba also referred to the specification and sequence listing of the opposed application when commenting on the claim 1 and observed that SEQ ID NO:1 to NO:6 are the CDR sequences of the variable regions of the heavy and light chains of ustekinumab.[93]

84. I have reviewed the sequence listing and description of the opposed application, and I accept the explanations of Professor Pavli and Professor Ciorba regarding how the sequences defined in claim 1 relate to those of ustekinumab. I interpret the scope of claim 1 includes ustekinumab itself and an antibody with the same six CDRs as ustekinumab. I note that the specification uses ustekinumab and Stelara® interchangeably and describes ustekinumab (Stelara®) as comprising a heavy chain having the amino acid sequence of SEQ ID NO:10 and a light chain having an amino acid sequence of SEQ ID NO:11.[94] I also note Stelara® is a commercial formulation of the antibody ustekinumab that was originally marketed by the applicant.[95] I consider the skilled person would understand that ustekinumab and Stelara® refer to an antibody having the six CDRs sequences defined in claim 1.

85. Professor Ciorba also explained that generally the CDRs inform the binding specificity and affinity of an antibody molecule and antibodies with the same six CDRs would be expected to have the same binding specificity and affinity as ustekinumab.[96]

86. During the oral hearing the opponent submitted that Professor Ciorba's statement (at [74] of his evidence) that "*[g]enerally speaking*, the amino acid sequence of the CDRs informs the binding specificity and affinity of an antibody", should not be understood as a universal proposition and that it will not always be true that antibodies with the same six CDRs would have the same specificity and affinity as ustekinumab.

87. This statement by Professor Ciorba was made in the context of providing the CGK about antibodies. Therefore, I consider it is reasonable to interpret the statement as meaning that it was generally known and accepted, at the priority date of the opposed specification, that the amino acid sequence of the CDRs informs the binding specificity and affinity of an antibody. My interpretation is consistent with the language used in the specification to describe the influence of CDRs on the binding capacity of an antibody. The specification states that "[i]n general, the CDR residues are directly and most substantially involved in influencing antigen binding".[97] I

[91] Pavli#1 at [281], [254] and cites the specification at page 31, paragraph 3 and the sequence listing of opposed application.
[92] Pavli #1 at [282].
[93] Ciorba at [252].
[94] The specification at page 3, lines 7 and 10; page 31, lines 16-18; page 89, line 1.
[95] Pavli # 1 at [112].
[96] Ciorba at [74], [252].
[97] The specification at page 18, lines 20-21.

also consider it is reasonable to interpret that an antibody with the same six CDR sequences as ustekinumab would be expected to have the same binding specificity and affinity as ustekinumab.

wherein after treating with the antibody, the subject is a responder to treatment by at least one measure of response to treatment

88. I consider that it is reasonable to interpret this phrase in the context that the method of treatment is for the *intended purpose* of effectively relieving or curing a subject with moderately to severely active UC. Firstly, I interpret the phrase to mean that after treating with the antibody, the *intention* is that the one or more subjects suffering from moderately to severely active UC show a measure of effectiveness to the treatment which is evaluated by at least one of the efficacy criteria defined. Secondly, I consider that the claim *does not* define a requirement that at least one of the defined efficacy criteria *will be* achieved in every case and that every subject must be sorted into one of these criteria. This is because in any given population there will be non-responders even in actual use. For the purposes of interpretation, I consider it is sufficient that *one or more* subjects show a clinical response to treatment, as defined by the efficacy criteria. My interpretation is consistent with the description in the specification where treatment with the antibody achieves a clinical response in some subjects but not others irrespective of the efficacy criteria being evaluated. My interpretation is also consistent with evidence of Professor Ciorba and Professor Pavli who both stated that for each medication which was approved for UC before the priority date of the opposed application, there were some patients who did not respond to the medication.[98]

selected from the group consisting of: (i) clinical remission based on at least one of the global definition of clinical remission with Mayo score ≤ 2 points with no individual subscore > 1 and the US definition of clinical remission with absolute stool number ≤ 3, rectal bleeding subscore of 0 and Mayo endoscopy subscore of 0 or 1, (ii) endoscopic healing with a Mayo endoscopy subscore of 0 or 1, (iii) clinical response based on the Mayo endoscopy subscore, (iv) mucosal healing, and (v) clinical response as determined by a decrease from baseline in the Mayo score by ≥30% and ≥3 points and a decrease from baseline in the rectal bleeding subscore ≥1 points or a rectal bleeding subscore of 0 or 1

89. Claim 1 defines five efficacy criteria by reference to indices for disease activity including a Mayo score, or a Mayo subscore. I have previously discussed the Mayo score and Mayo subscores.

Claims 2 and 3

90. Claims 2 and 3 are appended to claim 1. I have previously explained how the various sequences defined in claims 1, 2 and 3 relate to one another and noted that ustekinumab (Stelara®) comprises a heavy chain having the amino acid sequence of SEQ ID NO:10 and a light chain having an amino acid sequence of SEQ ID NO:11. Therefore, I interpret the antibody of claim 3 to be ustekinumab (Stelara®).

Claims 4 and 5

91. Claims 4 and 5 are ultimately appended to claim 1. I interpret the antibody of claim 4 to be in a pharmaceutical composition suitable for intravenous administration having a solution with the components defined in the claim. I interpret the antibody of claim 5 to be in a pharmaceutical

[98] Ciorba at [121]; Pavli #2 at [62].

composition suitable for subcutaneous administration having a solution with the components defined in the claim.

Claim 6

…***week 0 of the treatment***

92. Claim 6 is appended to claim 4. I consider the words of claim 6 define week 0 of the treatment as a time point when the first IV induction dose of the antibody is administered to the subject, this being at week 0 of the induction study. The antibody is administered at a dosage of 6.0 mg/kg body weight of the subject or 130 mg, 260 mg, 390 mg or 520 mg per administration. The antibody is in a pharmaceutical composition as defined in claim 4.

Claim 7

….week 8 of the treatment

93. Claim 7 is appended to claim 6. I interpret week 8 of the treatment to be eight weeks after the time point for the first IV dose defined in claim 6. In other words, a SC dose of the antibody is administered to the subject eight weeks after week 0 of the induction study. The antibody administered as a SC dose is in a pharmaceutical composition as defined in claim 5.

Claims 8 and 9

94. Each of claims 8 and 9 is appended to claim 7. I interpret the subject of claim 8 to have previously failed or was intolerant to at least one therapy from the five therapies defined in the claim or had demonstrated corticosteroid dependence.

95. I consider the words of claim 9 to define a treatment method that includes administering a maintenance dose every 8 weeks, or every 12 weeks, after the subcutaneous administration of the antibody at week 8 of the treatment defined in claim 7.

Claims 10 to 16

…44 weeks after week 0

96. Each of claims 10 to 16 is appended to claim 9. The applicant submitted:

> "The experts disagree on the meaning of the phrase '44 weeks after week 0' as used in claims 10-16 of the Opposed Application, although the Opponent also does not appear to press Prof. Pavli's contorted construction of this term in the OS…
>
> Prof. Pavli asserts that this phrase is a reference to '44 weeks after the first dose of ustekinumab (i.e. the IV induction dose referred to in claim 6)', despite acknowledging that this construction is inconsistent with the teaching of the Specification, and in particular 'differs from the format of the UNIFI Phase III clinical trial, in which patients were assessed at 44 weeks after the first maintenance dose of ustekinumab', and which is the subject of the Examples.

> Consistent with the evidence of Prof. Ciorba, a PSA would understand the term '44 weeks after week 0', when read in the context of the Specification as a whole, to mean '44 weeks after the first maintenance dose'. In particular, Prof. Ciorba states:
>
> > As Prof. Pavli notes, in the UNIFI Phase III trial, as reflected in Examples 1 and 2 of the Opposed Application, '*patients were assessed at 44 weeks after the first maintenance dose of ustekinumab*'. This is also consistent with Annex I, including Label Table 6, which refers to key efficacy measures at '*week 44; 52 weeks from initiation of the induction dose*'. I also note that elsewhere the claims state 'week 0 of the treatment' when referring to the first induction dose (see claims 6, 19, 33 and 34). Therefore, it is apparent to me that the reference to 'at least 44 weeks after week 0' (absent the qualifier 'of the treatment' following 'week 0') in claims 10-18 is a reference to at least 44 weeks after the first maintenance dose.
>
> It is also clearly the case that the feature '44 weeks after week 0' presented some linguistic difficulty that this terminology attempts to avoid. This is apparent from Figure 1, which shows that subjects who achieved a clinical response at week 8 and at week 16 of the Induction Study entered the Maintenance Study.
>
> The Applicant submits that the evidence of Prof. Ciorba should be preferred because it represents a whole of specification approach to claim construction that involves construing the claims in 'a practical, commonsense manner'."[99]

97. The opponent submitted during the oral hearing that it adopts Professor Pavli's interpretation of the phrase "44 weeks after week 0".[100] I also observe that Professor Pavli noted that "[presently amended claims 10-16] do not refer to 44 weeks of maintenance therapy, or 44 weeks after week 0 of maintenance therapy."[101]

98. I tend to be of the view that if the patentee had intended week 0 of claim 10-16 to be week 0 of the maintenance therapy, the words of the claims should have been chosen to reflect this qualification. I would be impermissibly importing a gloss from the figures and examples of the specification if I were to interpret "44 weeks after week 0" of claims 10-16 to be 44 weeks after week 0 *of the maintenance therapy*.

99. As there is no qualifier in the claims that week 0 is week 0 of the maintenance therapy, the plain meaning of the words indicates to me that week 0 of claim 10-16 is the time when the first IV induction dose of the antibody is administered to the subject. In other words, week 0 *of the treatment* as defined in claim 6. My interpretation would be consistent with the structure of the claim appendencies. Additionally, claim 10 defines "week 16 of the treatment" which I interpret to be a time 16 weeks after the first IV dose as defined in claim 6. Therefore, it seems reasonable to me that the same starting time point is intended for week 16 and week 0 in claim 10 and claims 11-16. I consider this to be a case where "the language of the claim must be understood to mean what it actually says".[102]

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[99] The AS at [83]-[87] citing Pavli #1 at [308], Pavli #2 at [130], Ciorba at [255] and the specification at page 75, lines 14-25.
[100] Pavli #1 at [308], Pavli #2 at [130].
[101] Pavli #1 at [308].
[102] *GlaxoSmithKline Consumer Healthcare Investments (Ireland) (No 2) Limited v Generic Partners Pty Limited* [2018] FCAFC 71; 131 IPR 384 at [121], [139].

100. I interpret the phrase "44 weeks after week 0" of claims 10-16 to be 44 weeks after the first IV dose of the antibody is administered to the subject as defined in claim 6.

Claim 11

…corticosteroid-free clinical remission

101. I consider the plain meaning of the phrase to be that the subject in clinical remission is not receiving concurrent corticosteroids to prevent the return of the symptoms of UC. I note that my interpretation of the phrase is consistent with the definition of this efficacy criteria provided in the specification.[103]

Claim 17

102. Claim 17 is a second independent claim to a method of treating moderately to severely active UC in a subject. I interpret the subject of claim 17 to be one or more individuals suffering from moderately to severely active UC and is not limited to a subject population. Additionally, I interpret the subject to be one who (a) had previously failed or was intolerant to at least one therapy from the five therapies defined in the claim, or (b) had demonstrated corticosteroid dependence. The therapies which the subject had failed or was intolerant to are (i) an anti-TNF (anti- Tumor Necrosis Factor), (ii) vedolizumab (an integrin antagonist). (iii) corticosteroids, (iv) azathioprine (AZA), and (v) 6 mercaptopurine (6 MP).

103. In the treatment method of claim 17, the subject is

- (a) administered an intravenous dose of an anti-IL-12/IL-23p40 antibody at week 0 of the treatment, and
- (b) administered a subcutaneous dose of the same anti-IL-12/IL-23p40 antibody at week 8 of the treatment.

I interpret the anti-IL-12/IL-23p40 antibody of claim 17 to be defined in identical terms as the antibody in claim 1, that is with identical CDR sequences on the heavy and light chain variable regions as those defined for claim 1. The quantity of the intravenous dose of anti-IL-12/IL-23p40 antibody at week 0 is defined in identical terms to the dose defined in claim 6. The quantity of the subcutaneous dose of anti-IL-12/IL-23p40 antibody at week 8 is defined in identical terms to the dose defined in claim 7. I interpret the scope of claim 17 to include an antibody with the same six CDRs as ustekinumab and includes ustekinumab itself.

104. The subject of claim 17 is defined to be a responder to treatment by at least one measure of response to treatment. For the same reasons as discussed for claim 1, I interpret that after administering the antibody, the intention is that one or more subjects suffering from moderately to severely active UC show a measure of effectiveness to the treatment which is evaluated by at least one of the efficacy criteria defined. Noting that there will be non-responders to treatment in any given population, as I previously discussed, I also consider that the claim does not define a requirement that at least one of the defined efficacy criteria will be achieved in every case and that every subject must be sorted into one of these criteria.

Claims 18-21

[103] The specification at page 78, lines 6-7.

105. Claims 18-21 are ultimately appended to claim 17 and define features in addition to those in claim 17. The antibody of claims 18 and 19 are defined in identical terms to the antibody in claims 2 and 3, respectively. The pharmaceutical composition of claim 20 is defined in identical terms as the composition of claim 4 which is suitable for intravenous administration. The pharmaceutical composition of claim 21 is defined in identical terms as the composition of claim 5 which is suitable for subcutaneous administration.

Claims 22-27

106. Claims 22-27 are appended to claim 17 and each appended claim defines that the intended response is that the subject demonstrates a specific efficacy criterion *by* week 16 of the treatment, that is any time before and until week 16 of the treatment. I interpret "week 16 of the treatment" to be 16 weeks after the subject is administered an intravenous dose of anti-IL-12/IL-23p40 antibody at week 0.

107. I consider that the skilled person would interpret "endoscopic healing" defined in claim 23 as improvement of the mucosal appearance as assessed by endoscopy. This is because endoscopic appearance of the mucosa is a component of the full Mayo score which is part of the CGK.[104]

108. I consider the plain meaning of "mucosal healing" defined in claim 25 means healing of the mucosa as assessed by any method well understood by the skilled person. This includes endoscopic assessment but is not limited to an improvement of the endoscopic mucosal appearance. For example, the specification describes histological healing of the mucosa and explains this is based on the Geboes score.[105] Professor Pavli stated that the Geboes score is widely known and generally accepted and used in Australia and overseas as criteria for UC clinical trials before the priority date.[106]

Claim 28

109. Claim 28 is appended to claim 17. I interpret the subject of claim 28 not to have shown a measure of effectiveness to treatment with the antibody, as evaluated by the five efficacy criteria defined in claim 17, by week 8 but does show a measure of effectiveness to treatment with the antibody by week 16. I interpret "week 8" and "week 16 of the treatment" in claim 28 to be the number of weeks after week 0 when the subject is administered an intravenous dose of anti-IL-12/IL-23p40 antibody.

Claim 29

110. Claim 29 is a third independent claim to a method of treating moderately to severely active UC in a subject. In the treatment method of claim 29, I interpret the subject is

- (a) administered an intravenous dose of an anti-IL-12/IL-23p40 antibody at week 0 of the treatment, and
- (b) administered a subcutaneous dose of the same anti-IL-12/IL-23p40 antibody at week 8 of the treatment, and

[104] Pavli # 1 at [91].
[105] The specification at page 67, lines 1-8.
[106] Pavli # 1 at [269].

- (c) provided a maintenance therapy for 44 weeks following the subcutaneous dose of the antibody administered in step (b), and
- (d) it is the intention that one or more subjects show a measure of effectiveness to the treatment which is evaluated by at least one of the efficacy criteria defined, noting that there will be non-responders to treatment in any given population.

111. I interpret the maintenance therapy of claim 29 to comprise an administration of a subcutaneous dose of the anti-IL-12/IL-23p40 antibody at a dosage of 90 mg per administration, once every 8 weeks or once every 12 weeks, in the 44-week period after week 8 of the treatment. Where the maintenance therapy is provided once every 8 weeks, the scope of claim 29 includes administration of a subcutaneous dose of the antibody 16, 24, 32 and 40 weeks after week 0 of the treatment. Where the maintenance therapy is provided once every 12 weeks, the scope of claim 29 includes administration of a subcutaneous dose of the antibody 20, 32 and 44 weeks after week 0 of the treatment. This is illustrated in Figure 1 of the opposed application.

112. I interpret the anti-IL-12/IL-23p40 antibody of claim 29 to be defined in identical terms as the antibody in claim 1, that is with identical CDR sequences on the heavy and light chain variable regions as those defined for claim 1. The quantity of the intravenous dose of anti-IL-12/IL-23p40 antibody administered at week 0 is defined in claim 29 in identical terms to the dose defined in claim 6. The quantity of the subcutaneous dose of anti-IL-12/IL-23p40 antibody administered at week 8 is defined in claim 29 in identical terms to the dose defined in claim 7. I interpret the scope of claim 29 to include an antibody with the same six CDRs as ustekinumab and includes ustekinumab itself.

Claim 30

113. Claim 30 is a fourth independent claim to a method of treating moderately to severely active UC in a subject. In the treatment method of claim 30, I interpret the subject is

- (a) administered an intravenous dose of an anti-IL-12/IL-23p40 antibody at week 0 of the treatment, and
- (b) administered a subcutaneous dose of the same anti-IL-12/IL-23p40 antibody at week 8 of the treatment, and
- (c) administered a maintenance therapy following the subcutaneous dose of the antibody administered in step (b), and
- (d) it is the intention that one or more subjects show a measure of effectiveness to the treatment which is evaluated by at least one of the efficacy criteria defined, noting that there will be non-responders to treatment in any given population.

114. I interpret the anti-IL-12/IL-23p40 antibody of claim 30 to be defined in identical terms as the antibody in claim 2; that is, with the heavy chain variable regions of amino acid sequence of SEQ ID NO:7 and light chain variable regions of amino acid sequence of SEQ ID NO:8. Since the amino acid sequences of SEQ ID NO:7 and SEQ ID NO:8 are, respectively, present in the heavy chain and the light chain of ustekinumab, I interpret the scope of claim 30 to include an antibody with the same six CDRs as ustekinumab and includes ustekinumab itself.

115. The quantity of the intravenous dose of anti-IL-12/IL-23p40 antibody administered at week 0 is defined in claim 30 in identical terms to the dose defined in claim 6. The quantity of the subcutaneous dose of anti-IL-12/IL-23p40 antibody administered at week 8 is defined in claim 30 in identical terms to the dose defined in claim 7.

116. I interpret the maintenance therapy of claim 30 to comprise an administration of an additional subcutaneous doses of the same anti-IL-12/IL-23p40 antibody as administered in step (b) which is provided at a dosage of 90 mg per administration. The antibody is administered once every 8 weeks, or once every 12 weeks, after week 8 of the treatment. Unlike claim 29, claim 30 does not limit the period of the maintenance therapy. For example, the scope of claim 30 includes (1) an additional subcutaneous dose of the antibody 16, 24, 32, 40, 48 or 56 weeks after week 0 of the treatment, where the maintenance therapy is provided once every 8 weeks, or (2) an additional subcutaneous dose of the antibody 20, 32, 44, 56 or 68 weeks after week 0 of the treatment, where the maintenance therapy is provided once every 12 weeks.

Novelty

117. It is a requirement of subsection 18(1) of the *Act* that the invention, so far as claimed in any claim, is novel. Subsection 7(1) states that an invention is taken to be novel unless it is not novel in the light of the prior art base as it stood before the priority date. For the purposes of the present consideration, the following kinds of information are relevant:

- Prior art information made publicly available in a single document; and
- Prior art information made publicly available in two or more related documents if the relationship between the documents is such that a person skilled in the relevant art would treat them as a single source of that information

118. It is well established that the general test for lack of novelty is the reverse infringement test. The classic formulation of this test is that given by Aickin J in *Meyers Taylor Pty Ltd. v Vicarr Industries Ltd.*:

> "The basic test for anticipation or want of novelty is the same as that for infringement and generally one can properly ask oneself whether the alleged anticipation would, if the patent were valid, constitute an infringement"[107]

119. This test is satisfied if the alleged anticipation discloses all the essential features of the invention as claimed.[108]

120. Australian courts have often identified the principles of the UK Court of Appeal in *The General Tire & Rubber Company v The Firestone Tyre and Rubber Company Limited*[109] (**the *General Tire* case**) as the criteria for determining anticipation by a prior publication. Most relevantly, to anticipate the patentee's claim the prior publication must contain clear and unmistakable directions to do what the patentee claims to have invented:

> "If the prior inventor's publication contains a clear description of, or clear instructions to do or make, something that would infringe the patentee's claim if carried out after the grant of the patentee's patent, the patentee's claim will have been shown to lack the necessary novelty, that is to say, it will have been anticipated. … if carrying out the directions contained in the prior inventor's publication will inevitably result in something being made or done which, if the patentee's patent were valid, would constitute an

[107] [1977] HCA 19 at [20]; 137 CLR 228 at 235.
[108] *Nicaro Holdings Pty Ltd v Martin Engineering Co* [1990] 91 ALR 513 at 517; 16 IPR 545.
[109] [1972] RPC 457 at 485-486.

> infringement of the patentee's claim, this circumstance demonstrates that the patentee's claim has in fact been anticipated.
>
> If, on the other hand, the prior publication contains a direction which is capable of being carried out in a manner which would infringe the patentee's claim, but would be at least as likely to be carried out in a way which would not do so, the patentee's claim will not have been anticipated … To anticipate the patentee's claim the prior publication must contain clear and unmistakeable directions to do what the patentee claims to have invented." [110]

121. In *Novozymes A/S v Danisco A/S*, Jessup J stated that the inevitability of outcome to which the *General Tire case* refers must be such as would arise from recourse to information referred to in subsection 7(1) of the *Act*:

> "the inevitability of outcome to which *General Tire* refers must be such as would arise from recourse to the *information* referred to in the section. At the expense of repetition, it is here useful to remind ourselves of what the Court of Appeal said in that case ([1972] RPC at 485-486):
>
> > … if carrying out the directions contained in the prior inventor's publication *will* inevitably result in something being made or done which, if the patentee's patent were valid, *would* constitute an infringement of the patentee's claim, this circumstance demonstrates that the patentee's claim has in fact been anticipated. [Emphasis added]
>
> This proposition is explicitly hypothetical. It is concerned not with what has happened or with what could have happened, but with what *would* have happened if the directions were carried out. As such, the proposition is in complete harmony with s 7(1), and with every other presently relevant aspect of the jurisprudence in this area. It is not the doing of it, nor even the ability to do it, that amounts to anticipation: it is the content of the information. If the information contains directions which, *if* carried out, *would* constitute an infringement of the patent in suit, the invention under the latter is not novel."[111] [Emphasis in original]

122. The Full Court in *Mylan Health Pty Ltd v Sun Pharma ANZ Pty Ltd* (**the *Mylan case***) held that a clinical trial protocol (the Accord Protocol) without scientific proof or substantiation anticipated a claimed invention:

> "We do not accept that a documentary disclosure containing an hypothesis cannot be an anticipatory disclosure that deprives an invention of novelty. In such a case the question, simply put, remains: what does the prior document disclose? The occasion on which, or the context in which, a particular documentary disclosure is made may well inform the interpretation of the document's content. But if, as a matter of interpretation, the document nonetheless discloses that which is later claimed as an invention, that disclosure will anticipate the invention and deprive it of novelty.
> …
> It is important to stress that validation of the ACCORD Protocol's hypothesis was certainly not required in order to achieve the equality of disclosure referred to in *Hill v*

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[110] Ibid.
[111] [2013] FCAFC 6 at [177]; 99 IPR 417.

> *Evans*. Looked at from a different perspective, it is not a requirement for a patentable invention that the invention, as claimed, be based on scientific proof or substantiation: *Generic Health Pty Ltd v Bayer Pharma Aktiengesellschaft* [2018] FCAFC 183; 267 FCR 428 at [135]. That being so, no greater requirement is imposed on a prior documentary disclosure in order for it to be anticipatory. What is required is that the prior document discloses that which is subsequently claimed as an invention. If that is disclosed, the invention cannot be new. If it should also be proved that the invention is not useful (for example, a claimed method of medical treatment is wholly or partly ineffective), then the patent can be challenged on that basis as well. But that raises a separate and distinct ground of invalidity."[112]

123. At the oral hearing the opponent relied on the following prior art citations to allege lack of novelty:

- The clinical trial record of the clinical trial titled *"A Study to Evaluate the Safety and Efficacy of Ustekinumab Induction and Maintenance Therapy in Participants With Moderately to Severely Active Ulcerative Colitis (UNIFI)"* and identifiable by ClinicalTrials.gov identifier NCT02407236 published on the ClinicalTrials.gov website on 13 August 2018 (**CTR 236**);

- Ochsenkühn, T., *et al* (2018) *"P759 Ustekinumab as rescue treatment in therapy-refractory or -intolerant ulcerative colitis"*, Journal of Crohn's and Colitis, Volume 12, Issue supplement 1, published on 16 January 2018 (**Abstract P759**);

- Poster titled *"Tu1713: Clinical outcomes with ustekinumab as rescue treatment in therapy-refractory or-intolerant ulcerative colitis: real world experience in a large single centre cohort"* presented at the AGA's annual conference, Digestive Disease Week, on 5 June 2018 (the **DDW Poster**); and

- Ochsenkühn, T., *et al* (2018) *"Tu1713: Clinical outcomes with ustekinumab as recue [sic] treatment in therapy-refractory or-intolerant ulcerative colitis: real worl [sic] experience in a large single centre cohort"*, Gastroenterology, Volume 154, Supplement 1, Issue 6, S-997, published in May 2018 (**Abstract Tu1713**); and

- Combinations of the above-mentioned documents with the approved Product Information for Stelara® (Ustekinumab) dated 27 February 2017 (the **Stelara 2017 PI**)[113]

124. While the OS alleged lack of novelty in light of information made publicly available by the conduct of Clinical Trial 236, the opponent did not make further submissions at the oral hearing concerning this allegation.[114] It is not clear to me the kinds of information encompassed by what the opponent referred to as "information made publicly available by the conduct of Clinical Trial 236". When I asked the opponent to clarify this issue at the oral hearing, the opponent did not elaborate on the matter. I understand the opponent does not pursue the allegation of lack of novelty outlined in paragraph [6](a)(v) of its written submissions filed 4 December 2024.

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[112] [2020] FCAFC 116 at [104]-[106]; 279 FCR 354.
[113] See also the OS at [6].
[114] The OS at [6](a)(v).

125. At the oral hearing, the opponent submitted that it does not rely on the Stelara 2017 PI as an independent novelty citation. This is because the opponent's primary argument concerning lack of novelty is that each of the four prior art citations, CTR 236, Abstract P759, the DDW Poster and Abstract TU1713, anticipate the claims of the opposed application. However, the opponent submitted that, if necessary and as a secondary argument, the Stelara 2017 PI can be read together with a prior art citation (for example, Abstract P759) and the two documents treated as a single source of information according to s 7(1)(b) of the *Act*.

126. I note that the Stelera 2017 PI was obtained from the Australian Public Assessment Reports (AusPAR) webpage, accessed through the Therapeutic Goods Australia (**TGA**) website, at URL: https://www.tga.gov.au/resources/auspar.[115] I also note that page 40 of the Stelera 2017 PI states that the "Date of the most recent amendment: 27 February 2017". It is not in dispute that the Stelera 2017 PI was publicly available before the priority date of the opposed application.

CTR 236

127. CTR 236 is a record of the UNIFI Phase III clinical trial published on the ClinicalTrials.gov website on 13 August 2018.[116] The clinical trial was performed to evaluate the efficacy and safety of ustekinumab in participants with moderately to severely active UC and was sponsored by Janssen Research & Development, LLC.

128. The official title of the study described in CTR 236 is "A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Protocol to Evaluate the Safety and Efficacy of Ustekinumab Induction and Maintenance Therapy in Subjects with Moderately to Severely Active Ulcerative Colitis".[117] The "Detailed Description" explains that the study consists of two studies: an 8 week "Induction study" and a 44 week "Maintenance study" where only those participants who demonstrated a response in the Induction study were eligible for the Maintenance study.[118] The table under the heading "Arms and Interventions" describes different groups participants were randomly assigned to in the trial.[119] Briefly, participants were grouped according to the dosage of ustekinumab administered to them, the type of administration (IV or SC) and when ustekinumab was administered. In the induction study, patients were administered one of IV placebo, IV ustekinumab at a dose of 130 mg or IV ustekinumab at a dose of 6 mg/kg. In the maintenance study, patients were administered one of SC placebo, SC ustekinumab at a dose of 90 mg every 8 weeks, or SC ustekinumab at a dose of 90 mg every 12 weeks.

129. The primary and secondary outcome measures (and the relevant endpoints) for the trial are described in the section under the heading "Outcome Measures".[120] The primary outcome measure for the Induction study is the number of participants with clinical remission (8 weeks after commencement of the Induction study) and for the Maintenance study is the number of participants with clinical remission among participants with clinical response in the Induction study (44 weeks after commencement of the Maintenance study). In both cases clinical remission is defined as "the global definition of Clinical remission is defined as Mayo score less than or equal to (<=) 2 points, with no individual subscore greater than (>) 1, for countries outside the

[115] Rohl #1 at [11]-[14].
[116] Rohl #1 at [5]-[6]; Pavli #1 at [177]; Ciorba at [137].
[117] CTR 236 at page 3.
[118] CTR 236 at pages 3-4.
[119] CTR 236 at pages 4-5.
[120] CTR 236 at page 5.

United Sates (US). For the US, Clinical remission is defined as absolute stool number <=3, a rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1."[121]

130. Each of the secondary outcome measures disclosed in CTR 236 evaluates the number of participants with a defined clinical response. Each clinical response is characterised in terms of a specific and measurable improvement compared to a baseline which I understand to be the severity of UC in a participant assessed at the commencement of the induction study (week 0).[122] The measure of improvement assessed for each clinical response is defined with reference to the Mayo score, endoscopic healing or IBDQ score.

131. The eligibility criteria for participants of the CTR 236 Phase III clinical trials are disclosed as including:

- a clinical diagnosis of UC at least 3 months before screening;
- having moderately to severely active UC, defined as Baseline (Week 0) Mayo score of 6 to 12, including a screening endoscopy subscore of the Mayo score ≥ 2 as determined by a central reading of the video endoscopy; and
- history of failure to respond to, or tolerate TNF antagonists, vedolizumab, oral corticosteroids, immunomodulators (6-mercaptopurine [6-MP] or Azathioprine [AZA]), or the participant had a history of corticosteroid dependence (that is, an inability to successfully taper corticosteroids without the return of UC).[123]

Consideration

132. As mentioned above, Professor Pavli and Professor Ciorba recognise Examples 1 and 2 of the specification as the induction study and the maintenance study, respectively, within a Phase III clinical trial for ustekinumab known as the UNIFI clinical trial.[124] In other words, the studies disclosed in CTR 236 are the same studies that are described in the present specification. However, I accept the applicant's observation that CTR 236 does not include any results from the UNIFI Phase III clinical trials.[125] I also note the observation by the opponent that the results from the UNIFI Phase III clinical trials were published in a journal article, referred to as the Sands 2019, after the priority date. The opponent relies on Sands 2019 as evidence of the result that will be inevitably achieved in following the dosage regime set out in CTR 236.[126] The opponent submitted that the "results" referred to in the claims of the opposed application are achieved by administering ustekinumab to UC patients in accordance with the dosage regimen disclosed in CTR 236.[127]

133. A relevant question, in the present circumstances, for the purposes of novelty is whether disclosure of the results of the Phase III clinical trials in CTR 236 is necessary to anticipate the claims of the opposed application.

134. The applicant submitted that:

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[121] Pavli #1 at [187]; Ciorba at [139].
[122] CTR 236 at page 6.
[123] Ibid.
[124] Pavli #1 at [259], Ciorba at [237].
[125] The AS at [129], citing Ciorba at [143], [212], [234], [271].
[126] The OS at [67] citing Sands, B.E., *et al* (2019) *"Ustekinumab as Induction and Maintenance Therapy for Ulcerative Colitis"*, The New England Journal of Medicine, Volume 381, No. 13, published 26 September 2019.
[127] The OS at Annexure A.

> "…method of treatment claims are characterised by their therapeutic purpose, such that there must be a *deliberate administration* of the claimed active agent *with the intention to treat* the claimed condition for a method of treatment claim to be infringed. By corollary, applying the "reverse infringement test" for novelty, the prior art must provide a disclosure that is equal to the deliberate administration of the relevant active agent with the intention to *treat* the specific condition defined in the claims in order to deprive the claims of novelty."[128] (emphasis in the original)

and

> "…for a claim to lack novelty the prior art must provide information that is equal to the invention that is claimed, in the sense that it must disclose the claimed invention with specificity and completeness. In other words, there must be a disclosure that is equal to an *intention to treat*. While a clinical trial disclosure may describe steps that, if followed in patients in need of treatment, *might* result in some patients being treated, the case law establishes that merely describing those steps does not rise to the necessary level of specificity and completeness required for anticipation (even in the event a treatment effect is later established); it is not "treatment" *in the patent sense* because it is not possible to form an intention to treat when it is not yet known whether a drug is even *capable* of treating a condition."[129] (emphasis in the original)

and

> "…the reason *Mylan* was decided differently was not because the prior art was a clinical trial protocol; it was because the clinical trial protocol included the disclosure of a 'reasoned hypothesis' that provided the necessary specificity and completeness to amount to 'treatment' *in the patent sense*."[130] (emphasis in the original)

and

> "…CTR 236 is a Phase III clinical trial protocol that, critically, does not contain any results, nor it does provide any rationale for why ustekinumab *will* treat moderately to severely active UC. It is a study designed to evaluate the safety and efficacy of ustekinumab in participants with moderately to severely active UC, and the first clinical trial of ustekinumab in this patient population. There is no teaching in CTR 236 of a 'reasoned hypothesis'; it is no more than a disclosure of a 'hypothesis to be tested'. Thus, CTR 236 discloses no more than the mere possibility of the use of ustekinumab in UC patients (cf. *Interpharma*) and therefore lacks the necessary specificity and completeness to amount to 'treatment' *in the patent sense*."[131] (emphasis in the original)

135. The opponent submitted:

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[128] The AS at [111].
[129] The APHS at [7].
[130] The APHS at [9].
[131] The APHS at [12], citing *InterPharma Pty Ltd v Hospira, Inc (No 5)*, (***InterPharma***), [2019] FCA 960, 149 IPR 182. At [10] of the APHS the applicant submitted that the Full Court in *Mylan* "clearly distinguished between a 'reasoned hypothesis' and a 'hypothesis to be tested, the latter not being sufficient to establish anticipation". At [11] of the APHS the applicant submitted that the clinical protocols in *InterPharma* and *Bristol-Myers Squibb Company v FH Faulding & Company Limited,* (***Faulding***), [2000] FCA 316, 97 FCR 524, merely disclosed 'a hypothesis to be tested'.

> "…it is difficult to conceive of a reason to give a patient a drug other than as a deliberate administration with an intention to treat their disease. All of the prior art documents disclose such a deliberate administration. That is all that is required for the claims here to be anticipated. To the extent any of the "results" in the claims need to be achieved, it is inevitable that they will be achieved."[132]

and

> "***Mylan***…did not endorse Mylan's submission that there was a relevant distinction between a 'hypothesis to be tested' and a reasoned hypothesis. Contrary to [the applicant's submissions in reply filed 07 February 2025 at [9]], the Full Court at [69] was setting out Mylan's submission, not adopting it. At [108]-[109], the Full Court rejected Mylan's submission that ***InterPharma*** *Pty Ltd v Hospira, Inc (No 5)* (2019) 149 IPR 182 was a relevant authority, and expressly noted that the correctness of Kenny J's factual conclusions in *InterPharma* as to the nature of the disclosure in that case was not before them."[133] (emphasis in the original)

and

> "…the disclosure in CTR 236 can be distinguished from the disclosure in *Interpharma*, which related to a "*Phase II single-centre trial involving only 24 patients*" – "*an early stage (phase II) clinical study*" involving "*a small number of patients and a single site*" (at [404] of *Interpharma*), where the expert evidence was that the purpose of the study was to see if the relevant drug (dexmedetomidine) "*may be worth investigating further as a potential agent*" (at [405] of *Interpharma*, and see generally the discussion at [399]-[424])."[134] (emphasis in the original)

and

> "The disclosure [in CTR 236] can be distinguished on a different basis from the prior art under consideration in *Bristol-Myers Squibb Company v FH* ***Faulding*** *& Company Limited* (2000) 97 FCR 524, where five pieces of prior art were reports of or articles on Phase I clinical trials of taxol, which were trials to establish a safe dosage limit of the compound. The Full Court explained at [67]:
>
> > *[…] Each of the trials reported in the articles referred to was an investigation directed towards finding a solution of the difficulties:* ***directed, particularly, to ascertaining safe dosage levels****. But, though methods falling within the claims of the patents were used in each trial,* ***none of the reports can be said to teach (a word which in this context encompasses direct, recommend and suggest) that which the petty patents claim****.* (emphasis in the original)
>
> As the Full Court in *Mylan* explained at [90], the reason that the Full Court in *Faulding* concluded that the reports of the Phase I trials did not anticipate is because they were disclosures about finding a solution to the difficulties of ascertaining safe dosage levels of

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[132] The ORS at [25].
[133] The OPHS at [2].
[134] The OPHS at [5].

> taxol, and did not disclose all the essential integers of the invention as claimed, which was directed to the use of taxol to treat cancer.
>
> Significantly, the Full Court in *Mylan* emphasised (at [90]) that the challenge to novelty in *Faulding* did not fail simply because the reports were about Phase I trials"[135] (emphasis in the original)

136. The question of whether CTR 236 is an anticipatory disclosure that deprives an invention of novelty is "what does the prior art disclose?"[136]

137. In summary, CTR 236 discloses Phase III clinical trial studies performed to evaluate the efficacy and safety of ustekinumab in participants with moderately to severely active UC. As previously discussed, ustekinumab is an antibody which the skilled person would understand as including the six CDRs as defined in independent claims 1, 17 and 29 of the opposed application. Since the studies disclosed in CTR 236 are the same studies that are described in the opposed application, the dosage regimen for administering ustekinumab to UC patients disclosed in CTR 236 is the same as that described in the present application and claimed in the claims.

138. CTR 236 discloses that the safety and efficacy of the Phase III Clinical trials are evaluated by determining the *number of participants with* (1) defined clinical remission criteria (primary outcome measure), and (2) defined clinical responses which are characterised with reference to the Mayo score, endoscopic healing or IBDQ score (secondary outcome measure). I understand that the defined clinical remission criteria and clinical responses to be specific and measurable results and that the Phase III Clinical trials of CTR 236 have been designed with the intended purpose of achieving these results. Therefore, CTR 236 discloses the intended specific and measurable results defined in the claims of the opposed application.

139. I observe that what is not disclosed in CTR 236 is the proportion of participants who demonstrate each of the intended and defined clinical remission criteria and clinical responses (primary and secondary outcome measures). However, the method of administering ustekinumab (that is, the form of administration and the dosage regimen) and the intended results (that is, the defined clinical remission criteria and clinical responses) are disclosed in CTR 236. Therefore, I consider the administration of ustekinumab disclosed in CTR 236 is a disclosure of a deliberate administration of the antibody to achieve the intended results which the clinical trials have been designed to evaluate.

140. In my view, the applicant's proposition which requires ustekinumab be known at the time of administration to be capable of treating UC is inconsistent with *Mylan* which found that it is not a requirement for the purposes of an anticipatory disclosure that the claimed invention be based on scientific proof or substantiation.[137] The applicant's proposition for an anticipatory disclosure is also inconsistent with *Warner-Lambert*, discussed above, which found that a claim will be infringed where a patient is administered a compound for the purposes of treating a condition even where the treatment is ineffective in the patient.[138]

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[135] The OPHS at [6]-[8].
[136] *Mylan* at [104].
[137] *Mylan* at [106] citing the principles used in *Generic Health Pty Ltd v Bayer Pharma Aktiengesellschaft* [2018] FCAFC 183; 267 FCR 428 at [135].
[138] [2016] FCA 1238; 122 IPR 17 at [129]-[131].

141. In the present case, the results of the clinical trials of CTR 236 establish the proportion of participants who achieved the intended and defined primary and secondary outcome measures (intended and defined clinical remission criteria and clinical responses). Therefore, I accept that the results provide a substantiation or validation of the safety and efficacy of administering ustekinumab to subjects with UC and prudent practitioners might well prefer to know the results of the trials before embracing a treatment method. However, validation of the safety and efficacy of administering ustekinumab to subjects with UC is not required for an anticipatory disclosure. It follows that, in the present case, regardless of the proportion of participants in the Phase III clinical trials established to demonstrate the defined primary and secondary outcome measures, there has been a disclosure of the method of treatment.

142. Additionally, I consider that CTR 236 contains a clear direction, recommendation or suggestion to deliberately administer ustekinumab with an intended purpose of treating a subject with UC by achieving the defined primary and secondary outcome measures. This is because regardless of how effective the method of treatment is established to be in the Phase III clinical trials, no further information, and therefore no further discovery, is required to achieve the equality of disclosure referred to in *Hill v Evans* for a skilled person to perform the invention in practice.[139] My consideration is consistent with how I interpret "method of treating" (see above) and the statements of Professor Pavli and Professor Ciorba that, as a matter of fact, not all patients will respond to a particular treatment. [140]

143. Therefore, I consider CTR 236 to be an anticipatory disclosure of the method of treating moderately to severely active UC as claimed in independent claims 1, 17 and 29.

144. Since I have found CTR 236 to anticipate claim 1 based on what the prior art itself document discloses, it follows I consider that the inclusion of a disclosure of a "reasoned hypothesis" is not necessary in the present circumstances. In any event, I agree with the opponent that a reasoned hypothesis did underlie the CTR 236 trial. The CTR 236 protocol summarises the position before 24 September 2018:

> "Data from completed Phase 2 studies of ustekinumab in Crohn's disease, along with the shared biology and the similar response to current treatments between Crohn's disease and UC, provide a substantial scientific and clinical rationale to justify a direct-to-Phase-3 approach to the study of ustekinumab in UC."[141]

145. Since validation of the safety and efficacy of administering ustekinumab is not required for an anticipatory disclosure, I consider it is not necessary to rely on Sands 2019 as evidence that the results of the Phase III clinical trials would be inevitably achieved in following the dosage regime set out in CTR 236. In any event, the results are inevitably achieved.

146. For the sake of completeness, I will now address the applicant's submissions that an "inevitable result exception" for method of treatment claims apply to the present claims as:

> "they are directed to a new method of treatment involving the administration of a known compound (ustekinumab or an antibody having the same six CDR sequences) for a

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[139] *Mylan* at [106]; *Hills v Evans* (1862) 45 ER 1195 at 2000.
[140] Pavli #1 at [118(a)] and Ciorba at [121].
[141] Annexure SJR-7 to Rohl #2 at page 33, third paragraph in non-bold font under heading "Synopsis".

> 'hitherto unknown and unexpected, but nevertheless useful, therapeutic use' in the *AstraZeneca* sense at [27] above (i.e., the treatment of UC by achieving).'"[142]

147. I agree with the opponent that the so-called "exception" discussed at [296] of *AstraZeneca AB v Apotex Pty Ltd* [2014] FCAFC 99 (***AstraZeneca***) applies to second medical use claims, where the prior use has been for a first medical use.[143] In other words, *AstraZeneca* dealt with a different situation where the prior art was for a treatment regimen, but the treatment was administered for some other purpose than the claimed purpose. [144] In the present case, CTR 236 discloses the administration of ustekinumab for treating UC, the purpose claimed in the claims of the opposed application.

148. The opponent submitted that:

> *"…Faulding, Merck* and *Mylan* are Full Court decisions in which a claim to a method of treatment was anticipated by prior art, notwithstanding the fact that the prior art preceded the results of Phase III clinical trials. It is clear from these authorities that there may be a suggestion to use a claimed method even before Phase III clinical trials are complete."[145]

I agree.

149. I conclude that independent claims 1, 17 and 29 of the opposed application lack novelty in view of CTR 236.

Claims 2, 3, 18, 19 and 30

150. From the discussions above, ustekinumab is an antibody which the skilled person would understand as including the sequences defined in claims 2, 3, 18, 19 and 30. Consequently, I conclude claims 2, 3, 18, 19 and 30 lack novelty in view of CTR 236.

Claims 4, 5, 20 and 21

151. The opponent submitted:

> "Since the skilled addressee would have understood that the ustekinumab which is administered is formulated as Stelara, being the only ustekinumab product available at the time, each of claims 4 and 5 is anticipated, because the IV and SC Stelara formulations had the claimed excipients, and CTR 236 discloses IV and SC administration."[146]

and

> "Professor Pavli explains that if he had been provided with or obtained any of CTR 236, Abstract P759, the DDW Poster and Abstract Tu1713, he would have read each of those

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[142] The APHS at [27]-[28], citing *AstraZeneca AB v Apotex Pty Ltd* [2014] FCAFC 99; (2014) 226 FCR 324 at [296] (***AstraZeneca***).
[143] The OPHS at [19].
[144] The ORS at [23].
[145] The OPHS at [23], citing *Bristol-Myers Squibb Company v FH Faulding & Company Limited,* [2000] FCA 316, 97 FCR 524 (***Faulding***), *Merck & Co Inc v Arrow Pharmaceuticals Ltd* [2006] FCAFC 91; (2006) 154 FCR 31; (***Merck***), and *Mylan Health Pty Ltd v Sun Pharma ANZ Pty Ltd*, [2020] FCAFC 116; 279 FCR 354 (***Mylan***).
[146] The OS at [68], citing Pavli #1 at [186], [288]-[291].

documents together with the Stelara 2017 Pl because Stelara was the only form of ustekinumab which had been approved by the regulator (and, in any event, of which he was aware) at the priority date. The Stelara PI discloses the excipients used in the Stelara formulation. If there were any doubt that any of these pieces of prior art anticipated claims 4 and 5, it is apparent that the claims are anticipated by reading the prior art together with the Stelara PI."[147]

152. The applicant submitted:

> "…CTR 236 does not disclose the formulation that was proposed to be used in the clinical trial, let alone the specific formulations claimed in each of claims 4, 5, 20 or 21. Contrary to the Opponent's assertion, the fact that a product containing ustekinumab (Stelara®) already existed on the market says nothing about the formulation that was used in CTR 236."[148]

and

> "Even if Prof. Pavli had drawn some common thread between the documents (e.g., that the impugned novelty citations refer to the same drug), that says nothing of the requirement under s 7(1)(b) that it is the documents themselves which must be shown to have a relationship such that they would be treated as a single source. Prof. Pavli's evidence is insufficient to satisfy the requirements of s 7(1)(b) and, to the contrary, the following factors tend against finding the documents would be treated as a 'single source':
>
> (i) There is no stated connection (i.e., cross reference) between the impugned documents. This is an important consideration. None of CTR 236, Abstract P759, Abstract Tu1713 and the Purported DDW Poster refers to the Stelara 2017 PI, and vice versa.
>
> (ii) There is no apparent connection between the authors of the Abstracts and the Purported DDW Poster on the one hand, and the Stelara 2017 PI on the other.
>
> (iii) The documents were not published simultaneously.
>
> (iv) The documents were published to different audiences in different circumstances. The Stelara 2017 PI was published in connection with the manufacture of Stelara®, whereas CTR 236 was published in an online archive containing other clinical trial data; the Abstracts were published in academic journals; and the DDW Poster is said to have been presented at a conference but has not been provided.
>
> (v) The documents concern the use of ustekinumab for different diseases. The Stelara 2017 PI addresses the use of ustekinumab for treating CD, psoriasis and psoriatic arthritis, whereas CTR 236, Abstract P759, Abstract Tu1713 and the Purported DDW Poster relate to the use of ustekinumab in UC patients."

[147] The OS at [68], citing Pavli #1 at [234].
[148] The AS at [141].

> Accordingly, it would not be appropriate to treat any of documents CTR 236, Abstract P759, Abstract Tu1713 and the Purported DDW Poster as a single source of information with the Stelara 2017 PI…"[149]

153. I accept Professor Pavli's evidence that before 24 September 2018, Stelara® was the only ustekinumab formulation approved by the TGA and marketed by Janssen.[150] However, I agree with the applicant that CTR 236 is silent about the formulation that was used in the UNIFI Phase III clinical trials. I also consider, for the reasons provided by the applicant, that the relationship between CTR 236 and the Stelera 2017 PI is insufficient for the documents to be considered as a single source of information.

154. Therefore, I consider CTR 236 does not disclose the specific formulations claimed in claims 4, 5, 20 and 21. Furthermore, the evidence filed does not established that the IV and SC formulations of Stelara® were part of the CGK such that the skilled person would have construed the disclosure of ustekinumab in CTR 236 to anticipate the specific formulations claimed in claims 4, 5, 20 and 21. Consequently, I conclude that the opponent has not established that each of claims 4, 5, 20 and 21 lacks novelty in view of CTR 236.

Claims 6-9

155. It is apparent that the dosage regimen defined in claims 6, 7 and 9 is disclosed in CTR 236. Additionally, the inclusion criteria for the UNIFI Phase III clinical trials disclosed in CTR 236 involved failure or intolerance to the agents claimed in claim 8. Consequently, I conclude that claims 6, 7, 8 and 9 lack novelty in view of CTR 236.

Claim 10

156. CTR 236 discloses that ustekinumab delayed responders (subjects who were not in clinical response to IV ustekinumab at induction week 8 but were in clinical response at induction week 16 after receiving ustekinumab 90 mg SC at induction week 8) were eligible to enter the maintenance study and administered a SC dose of ustekinumab every 8 weeks, or 12 weeks, through till maintenance week 44.[151] I consider it is reasonable to interpret this disclosure as saying that the clinical responses evaluated for the delayed responders included clinical remission at induction week 16 and then at maintenance week 44 (this being 52 weeks after week 0) since clinical remission is a primary outcome measure. Therefore, I consider CTR 236 discloses administering ustekinumab to delayed responders with an intention to achieve clinical remission at week 16 of the treatment and for continuation of clinical remission till week 52 after week 0. I also consider the intended time disclosed for continued clinical remission to fall within the scope of "at least 44 weeks after week 0". Therefore, I conclude that claim 10 lacks novelty in view of CTR 236.

Claim 11

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[149] The AS at [168]-[169].
[150] Pavli #1 at [186].
[151] These arms are titled "Induction study–Ustekinumab Nonresponders at Week 8", "Experimental: Maintenance Study–Ustekinumab 90mg SC every 12 weeks", "Experimental: Maintenance Study–Ustekinumab 90mg SC every 8 weeks (q8w)" and "Maintenance Study–Delayed Responder–Ustekinumab 90mg SC q8w", see CTR 236 at pages 4-5.

157. CTR 236 discloses a secondary outcome measure as "Number of Participants with Clinical Remission and not Receiving Concomitant Corticosteroids Among those Receiving Concomitant Corticosteroids at Maintenance Baseline".[152] I consider this disclosure to be saying that an intended purpose of the method of treatment is for the subject to be corticosteroid-free when in clinical remission.

158. The applicant submitted that the patient population of claim 11 "encompasses subjects who were not receiving concomitant corticosteroids at maintenance baseline (i.e., at week 0)".[153] I consider that the words of the claim do not place any limitations on the patient population and that the treatment status of the subject at the maintenance baseline is irrelevant. I also consider CTR 236 discloses administering ustekinumab to subjects with an intention to achieve corticosteroid-free remission which continues till week 52 after week 0. As previously discussed, the intended time disclosed for continued remission falls within the scope of "at least 44 weeks after week 0". Consequently, I conclude that claim 11 lacks novelty in view of CTR 236.

Claims 12-14 and 16

159. CTR 236 discloses that the secondary outcome measures (that is, clinical responses) of the maintenance study which are evaluated at maintenance week 44 include (1) a decrease from induction baseline in the Mayo score by ≥ 30% and ≥ 3 points, with either a decrease from induction baseline in the rectal bleeding subscore ≥ 1 or rectal bleeding subscore = 0 or 1; and (2) participants with endoscopic healing (this being, improvement in the endoscopic appearance of the mucosa and defined as Mayo endoscopic subscore = 0 or 1).[154] I consider the disclosure to teach a method of administering ustekinumab to subjects with an intention to achieve these clinical responses which continue till week 52 after week 0. I also consider the intended time disclosed for a continuation of the clinical response to fall within the scope of "at least 44 weeks after week 0". Consequently, I conclude claims 12-14 and 16 lack novelty in view of CTR 236.

Claim 15

160. CTR 236 does not disclose the identification of a subject having a normalisation of a biomarker, this being one or more of C-reactive protein, fecal lactoferrin and fecal calprotectin, as claimed in claim 15. However, Professor Pavli stated that outcome measures based on the C-reactive protein, fecal lactoferrin and fecal calprotein concentration tests are widely known, generally accepted and used as criteria or clinical endpoints for UC clinical trials before 24 September 2018.[155] Professor Pavli also stated that he would have expected some of the patients treated with ustekinumab according to the method disclosed in CTR 236 would have been identified as having a normalisation of one or more of the biomarkers as claimed in current claim 15.[156] I understand Professor Pavli to be saying that by administering ustekinumab to subjects according to the method disclosed in CTR 236, the clinical endpoint of current claim 15 would inevitably be achieved in some subjects.

161. I will discuss the issue of parameteritis shortly. For the present purposes, I consider the identification of a subject having a normalisation of one or more of the biomarkers as claimed in current claim 15 is not a feature that can provide a meaningful difference over what was disclosed

[152] CTR 236 at page 6.
[153] The AS at [142].
[154] CTR 236 at page 5.
[155] Pavli # 1 at [269].
[156] Pavli # 1 at [328(h)]

in the prior art but is "merely supplementary information" about the measure of success which the method of administering ustekinumab is intended to achieve.[157] Consequently, I conclude that claim 15 lacks novelty in view of CTR 236.

Claims 22-25 and 27

162. I consider it is reasonable to interpret CTR 236 as saying that the primary and secondary outcome measures used to evaluate the ustekinumab induction responders at week 8 are also used to evaluate the clinical responses of the delayed responders at week 16. These outcome measures include (1) clinical remission based on the global definition and the US definition, (2) a decreased from induction baseline in the Mayo score by ≥ 30% and ≥ 3 points, with either a decrease from induction baseline in the rectal bleeding subscore ≥ 1 or rectal bleeding subscore = 0 or 1; and (3) participants with endoscopic healing (this being, improvement in the endoscopic appearance of the mucosa and defined as Mayo endoscopic subscore = 0 or 1). Consequently, I conclude that that claims 22-25 and 27 lack novelty in view of CTR 236.

Claim 26

163. CTR 236 does not disclose the identification of a subject having a normalisation of a biomarker, these being one or more of C-reactive protein, fecal lactoferrin and fecal calprotectin, as claimed in claim 26. For the same reasons as discussed for claim 15, I consider the identification of a subject having the clinical endpoint as claimed in claim 26 is not a feature that can provide a meaningful difference over what was disclosed in the prior art but is "merely supplementary information" about the measure of success which the method of administering ustekinumab is intended to achieve.[158] Consequently, I conclude that claim 26 lacks novelty in view of CTR 236.

Claim 28

164. CTR 236 discloses that participants without a clinical response to induction treatment at week 8 but in clinical response at week 16 after receiving induction ustekinumab at week 8 (delayed responders) will receive ustekinumab 90mg subcutaneously every 8 weeks, beginning week 0 of the maintenance study through week 44.[159] Consequently, I conclude that claim 28 lacks novelty in view of CTR 236.

165. In summary, I find claims each of claims1-3, 6-19 and 22-30 lacks novelty in view of CTR 236. However, it has not been established that claims 4, 5, 20 and 21 lack novelty in view of CTR 236.

Abstract P759

166. Abstract P759 discloses a small-scale study that aimed to "assess the clinical outcomes achieved with ustekinumab as rescue treatment in therapy-refractory or intolerant UC". The "Background" of the Abstract P759 refers to ustekinumab as "commonly and successfully used in Crohn's disease". It also states that "…[p]re-approval trials are on-going and so far no clinical observation data on the use of ustekinumab in ulcerative colitis (UC) is available." [160]

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[157] *Otsuka Pharmaceutical Co., Ltd v Generic Health Pty Ltd (No 4)(**Otsuka**),* [2015] FCA 634; 113 IPR 191 at [321]-[322].
[158] *Otsuka* at [321]-[322].
[159] CTR 236 at page 5.
[160] Abstract P759 at page 1, paragraph under "Background".

167. Under the heading "Methods", the study is reported as "[a] retrospective data analysis…performed in 17 UC patients of our tertiary referral centre who received ustekinumab between 2016 and 2017 as rescue therapy." The primary outcome of the study is disclosed as "the achievement of clinical remission at 3 and 6 months. Clinical remission was defined as score of ≤5 points in the modified Truelove and Witts colitis activity index (CAI)."[161]

168. Professor Pavli acknowledged the names as a reference to Dr Sidney Truelove and Dr Leslie Witts who, in 1955, published a seminal paper regarding the use of steroids in the treatment of UC which drastically improved the prospects of patients with the disease. Professor Pavli also stated that he was aware that, before 24 September 2018, Dr Truelove and Dr Witts had published a classification of disease severity for UC but he had typically used one or more of the various Mayo scores to assess the severity of a patient's disease.[162] Therefore, I understand the disease index disclosed for assessing the severity of UC in Abstract P759 differs from that used to define the efficacy criteria (outcome measures) in the claims of the opposed application.

169. Abstract P759 discloses that:

> "A total of 17 UC patients were treated with ustekinumab. All patients (17/17) previously had been steroid refractory or dependant and had recently failed all of the following drugs: purine-analogues, anti-TNF-antibodies and anti-integrin-antibodies. Of those, 41% (7/17) had failed infliximab and either golimumab or adalimumab, and 29% (5/17) had also failed i.v. ciclosporine."[163]

and

> "To all patients ustekinumab was provided as a rescue treatment after colectomy had been offered to them as only other option."[164]

170. It is apparent from the paragraphs quoted above that the only remaining options for the 17 UC patients were surgery or ustekinumab. This understanding is consistent with that of Professor Pavli and Professor Ciorba.[165] I note that Professor Pavli's statement that "the only remaining options for these patients were surgery or an unapproved therapy (specifically, here, ustekinumab).[166]

171. Both Professor Pavli and Professor Ciorba referred to the use of ustekinumab in Abstract P759 as "off-label" use of ustekinumab. Professor Pavli explained that off-label usage of a medication involves prescribing a patient a drug which has been approved by the TGA, or the relevant regulatory body in other countries, but not for the disease in question (e.g., prescribing a drug which has been approved for use in the treatment of rheumatoid arthritis for use in patients with CD or UC).[167] Professor Ciorba described the off-label use of ustekinumab in Abstract P759 to correspond to a scenario which he categorised as high-risk, without Phase III clinical data, and

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[161] Abstract P759 at page 1, paragraph under "Methods".
[162] Pavli #1 at [195].
[163] Abstract P759 at page 1, paragraph under "Results".
[164] Abstract P759 at page 1, paragraph under "Methods".
[165] Pavli #1 at [197], Ciorba at [146].
[166] Pavli # 1 at [197].
[167] Pavli # 1 at [137], [198].

where there is no way of predicting whether or not the off-label use of the medication is safe or efficacious in relation to the indication of interest.[168]

172. The "Results" section of Abstract P759 discloses:

> "At the start of the rescue therapy, 65% of patients (11/17) had moderately or severely active disease and 35% (6/17) were in remission, but had intolerable side effects under TNF or integrin blocking treatment, which had to be stopped. Therefore, the CAI at the start of the therapy ranged between 1 and 11 with a median of 8…"[169]

173. I understand that 11 of the 17 patients had moderately or severely active UC before treatment with ustekinumab and the remaining 6 of the 17 patients were in remission due to treatment with an anti-TNF-antibody or an anti-integrin-antibody. However, the antibody treatments had to be stopped because of intolerable side effects.

174. The "Results" section states:

> "All patients received *ustekinumab as approved for Crohn's disease* (6 mg/kg body weight as an infusion and 90 mg ustekinumab as s.c. injection every 8 weeks). Median follow-up was 27 weeks (range: 15–40). In two patients therapy was stopped due to refractory disease at months 6 and 24 and in 1 patient, therapy was stopped due to drowsiness at week 4. All 3 patients underwent colectomy. Median CAI at 4 weeks was 5 points (range 1–8). Median CAI at 3 months was 4.5 points (range 0–9). Median CAI at 6 months was 2 points (range 0 7) Including [sic] the three drop outs, clinical remission was achieved in 65% (11/17) at 1, 3, and 6 months, whereas only 35% (6/17) of patients were in remission at the start of the study."[170] (emphasis added)

175. I understand that all patients received ustekinumab in accordance with the approved dosage regimen for CD, this being 6 mg/kg body weight as an infusion and 90 mg ustekinumab as a SC injection every 8 weeks. My understanding is consistent with that of Professor Pavli.[171]

176. I also understand that treatment with ustekinumab was unsuccessful in 3 of the 17 UC patients, and colectomy was required in all 3 patients. Including these 3 patients, clinical remission was reported in 11/17 patients at 1, 3 and 6 months, compared to 6/17 patients in remission before ustekinumab therapy.

177. The "Conclusions" section states:

> "Ustekinumab was effective as rescue medication in therapy refractory or intolerant UC in a large IBD referral center. It seems possible that large ongoing trials will confirm our findings and ustekinumab could become a new therapeutic option for refractory UC."[172]

Consideration

Is the reference in Abstract P759 to ustekinumab a reference to Stelara®?

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[168] Ciorba at [101], [102], [146],
[169] Abstract P759 at pages 1-2, paragraph under "Results".
[170] Abstract P759 at page 2, paragraph under "Results".
[171] Pavli # 1 at [201].
[172] Abstract P759 at page 2, paragraph under "Conclusions".

178. At the oral hearing the opponent submitted that the reference in Abstract P759 to the administration of "…*ustekinumab as approved for Crohn's disease*…" (section reproduced above in context) is a reference to administration of Stelara® because (1) Stelara® was the approved medication for CD and (2) the dosage regime approved for CD (and disclosed in Abstract P759) was in accordance with the Stelara® product.

179. Professor Pavli stated that:

> "…off-label usage of a medication involves prescribing a patient a drug which has been approved by the TGA (or, for those in other countries, the relevant regulatory body in those countries) but not for the disease in question. I therefore understand the references to the administration of ustekinumab in Abstract P759 to be references to the administration of Stelara, being the IV and SC formulations which had obtained regulatory approval before 24 September 2018, and the only ustekinumab formulations of which I was aware before that time."[173]

180. I consider it is reasonable to infer that a skilled person would read the references to ustekinumab in Abstract P759 in the context that ustekinumab was being administered as an off-label treatment (or rescue treatment) and construed in view of the CGK. I consider the evidence establishes that it was part of the CGK that ustekinumab (Stelara®) was approved for treating CD by the FDA in 2016 and by the TGA in 2017.[174] I also accept Professor Pavli's evidence that Stelara® was the only ustekinumab formulation at the time (between 2016 and 2017) the patients received the off-label treatment.

181. Therefore, I consider that a skilled person would understand that the reference in Abstract P759 to the administration of "…*ustekinumab as approved for Crohn's disease* (6 mg/kg body weight as an infusion and 90 mg ustekinumab as s.c. injection every 8 weeks)…" is a reference to administration of Stelara® and with the IV and SC dosage regime as approved, by the relevant regulatory body, for CD.

Is off-label use of ustekinumab disclosed in Abstract P759 a method of treatment?

182. The applicant submitted that:

> "…a disclosure of off-label use of a drug cannot deprive a claim of novelty unless it is accompanied by a disclosure of a 'reasoned hypothesis' that the drug *will* treat the condition. Otherwise, it is no more than a disclosure that a drug might treat the condition and lacks the necessary specificity and completeness to deprive the claims of novelty.[175] (emphasis in original)

and

> "…the Opponent has conflated a *hope* that a drug *might* treat a disease with a *reasonable belief* that it *will* treat the disease. As Prof. Ciorba notes, administering a drug off-label in the circumstances described in the Abstracts and the DDW Poster is a 'Hail Mary'; a desperate, last-resort attempt to avoid surgery in circumstances where all approved

[173] Pavli #1 at [198].
[174] Ciorba at [75], [170]; Pavli #1 at [113]
[175] The APHS at [19].

> options have failed. Such desperate measures, taken in the *hope* that a condition *might* be treated, cannot be characterised as a deliberate administration for the purpose of "treating" *in the patent sense*, as contemplated by the High Court in *Sanofi."*[176] (emphasis in original)

and

> "…the Applicant does not suggest that 'off-label use is inherently incapable of anticipating'. Indeed, the evidence of Prof. Ciorba supports that off-label use can be characterised as 'treatment' under certain circumstances, namely, where a detailed understanding of the safety and efficacy profile of the drug has been established based on a large volume of real world data gathered over many years. This is not the case with the small number of off-label uses described in the Abstracts or the DDW Poster (and in the absence of a placebo control), the results of which are equivalent to the placebo effect observed in UC clinical trials."[177]

183. The opponent submitted:

> "…A skilled addressee reading each of the reports of off-label use would have appreciated that the relevant patients were treated by those uses. Each report contained a direction, recommendation or suggestion, in the sense identified by the Full Court in *Faulding* at [84]….
>
> The suggestion at JSR [21]-[24] that a report of a Phase I trial will not anticipate in the absence of a reasoned hypothesis does not reflect the observations of the Full Court in *Mylan* at [90]. The only relevant question is whether the prior art discloses that which is claimed: that is, in this case, the administration of ustekinumab to treat UC…."[178]

184. I agree with the opponent that the relevant question of whether Abstract P759 is an anticipatory disclosure that deprives an invention of novelty is "what does the prior art disclose?"[179]

185. Even though ustekinumab was administered as an off-label treatment in Abstract P759 and to avoid surgery, it is apparent that ustekinumab is being used with the intended purpose to relieve or cure a patient with moderately to severely active UC. Abstract P759 relates to a small group of patients who were deliberately administered ustekinumab and also reports the proportion of patients who achieved clinical remission as an indication of the efficacy of ustekinumab therapy.

186. The applicant submitted:

> "…retroactive studies of off-label use such as that described in Abstract P759 are subjective in nature, rely heavily on hindsight assessment and are not generalisable to the broader population of UC patients…Abstract P759 also contains myriad deficiencies that warrant further caution being exercised in drawing any conclusions from this document. These deficiencies include:
>
> (i) …**retrospective data analysis**…

[176] The APHS at [20].
[177] The APHS at [21].
[178] The OPHS at [17]-[18].
[179] *Mylan* at [104].

(ii) …**lacks a control (e.g., placebo) group, blinding and randomisation**…
(iii) …**small sample size**…
(iv) …**lacks important participant information**…
(v) …**lacks any statistical hypothesis testing**…"[180] (emphasis in the original)

187. Professor Pavli stated:

> "Retrospective studies provide an opportunity to share knowledge regarding off-label treatment with a medication for a particular indication before, and potentially many years before, it is approved by a regulatory authority for that indication. Before 24 September 2018, I, and based on my discussions with my colleagues and to my observation other gastroenterologists in Australia (and overseas), considered retrospective studies and the reporting of retrospective studies to be an important component of the sharing of medical knowledge and the development of new approaches to the treatment of IBD and used the information from these studies to inform my (or their) clinical practice…."[181]

188. I accept that (i) there may be limitations regarding the conclusions that can be drawn from retrospective studies, and (ii) these studies are still important in the development of approaches to the treatment of IBD. However, even if there are limitations, these limitations do not undermine the disclosure in Abstract P759. Consequently, I consider the off-label use of ustekinumab disclosed in Abstract P759 is a method of treatment that is relevant for the purposes of assessing novelty.

Can the specific efficacy criteria or clinical endpoints defined in the claims confer novelty?

189. The opponent submitted that the clinical endpoints and the length of the maintenance treatment recited in the claims of the opposed application amount to "parameteritis" in the sense that the recitations are an attempt to re-patent the prior art by limiting the claims by reference to a parameter not specifically mentioned but nonetheless encompassed in the prior art, and therefore do not reflect a new use. [182] The opponent relies on the findings of Yates J at first instance in *Otsuka Pharmaceutical Co., Ltd v Generic Health Pty Ltd (No 4)(**Otsuka**),* and the comments of Beach J on appeal in *Otsuka Pharmaceutical Co., Ltd v Generic Health Pty Ltd (No 2)(**Otsuka Full court Decision**)*.[183]

190. The applicant submitted that the clinical endpoints have a technical effect, are part of the invention, and are directly related to a claimed advantage of the invention. The applicant relies on the considerations of Nicholas J in *Neurim Pharmaceuticals 91991) Ltd v Generic Partners Pty Ltd (No 5) (**Neurim**)*:

> "In *Neurim*, Nicholas J considered whether the 'inevitable result exception' discussed in *AstraZeneca* applies in the case of a subset of a previously disclosed use or method. In *Neurim*, the claims at issue were directed to a prolonged release formulation of melatonin treatment of 'primary insomnia characterized by non-restorative sleep and improving the restorative quality of sleep in said patient', whereas the prior art related to use of

[180] The AS at [151].
[181] Pavli # 2 at [15].
[182] The OS at [54]-[57]; the ORS at [28.b].
[183] *Otsuka,* [2015] FCA 634; 113 IPR 191 at [320]-[327]; *Otsuka Full court Decision,* [2016] FCAFC 111, 120 IPR 431 at [115].

prolonged release formulations of melatonin for treating various indications, including insomnia and improving sleep quality.

Nicholas J rejected the respondent's characterisation of the claims directed to a narrower use than the prior art as 'parameteritis'. In that regard, his Honour considered that the newly claimed features 'have a technical effect, are part of the invention, and are directly related to a claimed advantage of the invention' (i.e., were more akin to a selection invention). Accordingly, his Honour considered that the claims are novel (and involve an inventive step) because they are directed to a new therapeutic use and 'it was not an inevitable result of the prior use of melatonin that it had been or would be used as such a treatment'" [184]

191. The applicant also submitted:

"…each of the above Clinical Endpoints requires endoscopic assessment of the subject, which is the most reliable and objective measure of disease activity in UC patients. In contrast, a classification of 'remission' according to the modified Truelove and Witts CAI, also known as the Lichtiger CAI, is less reliable and more subjective than each of the Clinical Endpoints recited in the present claims because it does not involve endoscopic assessment. Further, there are differing reports in the literature about what qualifies as 'clinical remission' according to the modified Truelove and Witts CAI, ranging from a score of 2 to 5 (inclusive). Accordingly, it is entirely possible that a patient could meet the criteria for remission according to the modified Truelove and Witts CAI but fail to meet the more reliable and objective Clinical Endpoints recited in the claims of the Opposed Application." (emphasis in the original)[185]

192. The opponent responded:

"…the clinical endpoints are mere parameteritis. Janssen does not suggest (nor could it suggest) that there is any difference between the method disclosed in the Application and the method disclosed in the prior art which would mean that the use of ustekinumab in the claims would achieve hitherto unattainable results: its case is not that the Application discloses a new therapeutic use, but merely that the efficacy of the previously disclosed use can be more precisely measured. The endpoints do not have a 'technical effect'…

That being the case, the fact that the Application uses a more '*reliable and objective measure of disease activity*' than those reported in the prior art is not to the point. The identification of the specific clinical endpoints which are achieved by the use of ustekinumab is not a '*free- standing essential feature of the invention which is to be considered as meaningfully adding*" to what was disclosed by the prior art. When the question of novelty is considered (as it must be) as a question of substance, rather than mere claim form, these endpoints are "*merely supplementary information*": see, analogously, *Otsuka Pharmaceutical Co Ltd v Generic Health Pty Ltd (No 2)* (2016) 120 IPR 431 at [173]-[176]."[186] (emphasis in the original)

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[184] The AS at [109]-[110], [147], citing *Neurim*, [2024] FCA 360 at [331].
[185] The AS at [149], citing Ciorba at [53], [57], [59], [140], [214]; Pavli #2 at [22]; Ciorba at [67], [150], [160], [214]; Ciorba at [162], [210] and Ciorba at [150], [161].
[186] The OPHS at [25].

193. I have previously found that the disease index used for assessing the severity of UC in Abstract P759 differs from that used to define the efficacy criteria in the claims of the opposed application. However, it is apparent that the form and dosage regimen of administering ustekinumab disclosed in Abstract P759 – that is, 6 mg/kg body weight as an infusion and 90 mg ustekinumab as a SC injection every 8 weeks – is the same as that disclosed in the opposed application and as defined in some of the claims, for example, claims 9, 17 and 30. Therefore, I agree with the opponent that the opposed application does not disclose a new therapeutic use, but merely that the efficacy disclosed in Abstract P759 can be more precisely measured.

194. Regardless of whether a subject is (1) identified as having a specific clinical endpoint as defined in the claims of the opposed application, or (2) identified as having achieved clinical remission according to the modified Truelove and Witts CAI, the method of treatment disclosed in Abstract P759 is the same as that defined in the current claims. The intended purpose of the method of both the prior art and the current claims is to effectively treat moderately to severely active UC. I consider that by administering ustekinumab according to the method disclosed in the prior art, the specific clinical endpoints defined in the current claims would inevitably be achieved in one or more subjects. The facts of the opposed application are distinguished from those in *Neurim.*

195. Therefore, while the specific clinical endpoints can be considered "information given as part of the definition of the invention in a claim [that] is new information" – in the sense that the specific clinical endpoints are not disclosed in Abstract P759 – I consider the endpoints, as defined in the present case, are not features that can provide a meaningful difference over what was disclosed in the prior art but are "merely supplementary information" about the measure of success which the method of administering ustekinumab is intended to achieve.[187] Consequently, I consider the specific clinical endpoints cannot confer novelty.

196. However, I consider the length of the maintenance treatment recited in claim 29, this being 44 weeks, does specify the duration of the maintenance therapy and is therefore a limitation on the dosage regimen. Consequently, I consider the length of the maintenance treatment is a limitation on the claim and can confer novelty.

Claims 1, 2, 3, 17, 18, 19, 29 and 30

197. From the discussions above, ustekinumab is an antibody which the skilled person would understand as including the sequences defined in claims 1, 2, 3, 17, 18, 19, 29 and 30 of the opposed application.[188] Since I have found that the specific clinical endpoints cannot confer novelty to the method of administering ustekinumab, I conclude that claims 1, 2, 3, 17, 18, 19 and 30 are not novel in view of Abstract P759.

198. However, Abstract P759 does not disclose administering 90 mg ustekinumab as a SC injection once every 8 weeks for 44 weeks. Therefore, Abstract P759 does not disclose a maintenance therapy provided for 44 weeks. Since I consider the length of the maintenance treatment is a limitation on the method of administering ustekinumab, I conclude that it has not been established that claim 29 lacks novelty in view of Abstract P759.

Claims 4, 5, 20 and 21

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[187] *Otsuka* at [321]-[322].
[188] Pavli #1 at [282]; Ciorba at [252].

199. I have previously found that a skilled person would understand that the reference in Abstract P759 to the administration of "…*ustekinumab as approved for Crohn's disease* (6 mg/kg body weight as an infusion and 90 mg ustekinumab as s.c. injection every 8 weeks)…" is a reference to administration of Stelara® and with the IV and SC dosage regime as approved, by the relevant regulatory body, for CD. The IV formulation of Stelara® comprises a solution with the excipients claimed in claims 4 and 20, as a matter of fact.[189] The SC formulation of Stelara® comprises a solution with the excipients claimed in claim 5 and claim 21, as a matter of fact.[190] Consequently, I conclude that claims 4, 5, 20 and 21 are not novel in view of Abstract P759.

Claims 6-9

200. It is apparent that the dosage regimen defined in claims 6, 7 and 9 is disclosed in Abstract P759. Additionally, all patients of the study in Abstract P759 were disclosed as intolerant or refractory to purine analogues, TNF antibody therapy and vedolizumab. Consequently, I conclude that claims 6, 7, 8 and 9 lack novelty in view of Abstract P759.

Claims 10-16

201. Abstract P759 discloses that all patients received 6 mg/kg body weight ustekinumab as an infusion and 90 mg ustekinumab as a SC injection every 8 weeks. The median follow-up period was disclosed as 27 weeks with a range of 15-40 weeks. Relevantly, there is no disclosure that clinical remission continues at least 44 weeks after the first IV dose of ustekinumab. Consequently, I conclude that it has not been established that claims 10-16 lack novelty in view of Abstract P759.

Claims 22-28

202. Abstract P759 discloses that clinical remission was achieved in 65% patients at 1, 3 and 6 months. I understand that clinical remission was achieved in some of the patients at week 4, week 12 and week 24 after the first IV dose of ustekinumab. Therefore, Abstract P759 discloses that clinical remission was achieved in some patients by week 16 after the first IV dose of ustekinumab. Consequently, I conclude that claims 22-25, 27 and 28 lack novelty in view of Abstract P759.

203. Abstract P759 does not disclose identification of a subject having a normalisation of one or more of the biomarkers claimed in claim 26. For the reasons previously discussed, I consider the identification of a subject having the clinical endpoint as claimed in claim 26 is not a feature that can provide a meaningful difference over what was disclosed in the prior art but is "merely supplementary information" about the measure of success which the method of administering ustekinumab is intended to achieve.[191] Additionally, I consider that administering ustekinumab according to the method disclosed in Abstract P759 would inevitably achieve this clinical endpoint in one or more subjects. Consequently, I conclude that claim 26 lacks novelty in view of Abstract P759.

204. I conclude that claims 1-9, 17-28 and 30 lack novelty in view of Abstract P759. However, it has not been established that claims 10-16 and 29 lack novelty in view of Abstract P759.

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[189] See Stelara 2017 PI filed as Annexure VK-4; Kayser at [44]-[49].
[190] See Stelara 2017 PI filed as Annexure VK-4; Kayser at [50]-[55].
[191] *Otsuka* at [321]-[322].

DDW Poster

205. At the oral hearing the applicant submitted that I cannot be certain that DDW Poster contains the same information as the actual poster that was exhibited at the Digestive Disease Week conference (the **DDW conference**) on 5 June 2018. The applicant also submitted that since information regarding the poster was obtained by Mr Rohl in a telephone conversation with Professor Ochsenkühn, the information is hearsay evidence and DDW Poster is not admissible as a prior art citation.

206. Mr Rohl has stated in evidence that Professor Ochsenkühn had informed him in a telephone conversation that a printed poster containing the same information as the DDW Poster was displayed on the 5 June 2018 at the DDW conference. Mr Rohl also stated that Professor Ochsenkühn also informed him that there was no limitations or restrictions on the use of the content of the poster by anyone who saw or read the poster, and that any attendee of the DDW conference was able to read the information in the displayed poster.[192]

207. While the evidence concerning the DDW Poster before me is not directly from Professor Ochsenkühn, I find no reason to doubt the veracity of Mr Rohl's evidence. In my view, it is reasonable to consider that the DDW Poster contains the same information as the printed poster that was displayed by Professor Ochsenkühn at the DDW conference on the 5 June 2018. I also consider that the actual poster was publicly available because anyone who saw the poster could use the information contained in the poster without restriction. It follows that I consider that the DDW Poster to be a copy of a publicly available document (the actual printed poster) containing information that was publicly available on 5 June 2018. Therefore, in my view, the DDW Poster is a prior art document for the present purposes of assessing novelty.

208. The authors of the DDW Poster are the same as the authors of Abstract P759. The DDW Poster appears to expand on the study described in Abstract P759 as it relates to 19 patients (rather than 17) and up to 9 months treatment (rather than 6 months' treatment). Otherwise, the contents of the DDW Poster are very similar to that of Abstract P759.

209. The study disclosed in the DDW Poster is described as a retrospective data analysis performed on 19 patients between 2016 and 2017. All patients are described to be "steroid-refractory or -dependant [sic] and had recently failed or were intolerant to all of the following drugs: purine-analogues, anti-TNF-antibodies and anti-integrin-antibodies". Some had failed with two anti-TNF-antibodies or cyclosporine.[193]

210. The DDW Poster states that ustekinumab was provide as a rescue treatment after colectomy had been offered to them as the only other option. I understand the only options offered to patients were colectomy or ustekinumab therapy. My understanding is consistent with that of Professor Pavli.[194]

211. The DDW Poster also states:

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[192] Rohl #1 at [15]-[17].
[193] DDW Poster, first and second paragraphs under the heading "Methods".
[194] Pavli #1 at [220].

> "The primary outcome was achievement of clinical remission at 3, 6 and 9 months. Clinical remission was defined as score of ≤5 points in the Lichtiger score (=modified Truelove and Witts colitis activity index, CAI)."

212. I understand that the disease index disclosed for assessing the severity of UC in the DDW Poster is the same as that disclosed in Abstract P759 but differs from that used to define the efficacy criteria (outcome measures) in the claims of the opposed application.

213. The DDW Poster states:

> "At the start of rescue therapy, 63,2% of patients (12/19) had moderately or severely active disease and 36,8 (7/19) were in remission, but had intolerable side effects under TNF- or integrin blocking treatment, which therefore had to be stopped."[195]

214. I understand the paragraph quoted above to mean that 12 of the 19 patients had moderately or severely active disease before ustekinumab treatment and the remaining patients were in remission due to therapy with anti-TNF-antibodies and anti-integrin-antibodies. However, the antibody therapies were associated with unacceptable side effects such that it was not viable to continue this approach with the patients. I understand the antibodies were stopped before ustekinumab treatment. My understanding is consistent with that of Professor Pavli.[196]

215. The DDW Poster states:

> "A total of 19 UC patients were treated with ustekinumab and all patients received ustekinumab as approved for Crohn's disease (6 mg/kg body weight as an infusion and 90 mg ustekinumab as s.c. injection every 8 w):
>
> - In 4 patients, therapy was stopped due to refractory disease at 2 months (one patient) and 6 months (three patients) and in 1 patient therapy was stopped due to drowsiness at week 4. In one woman, breast cancer was diagnosed after the induction dose, she received surgery, chemo- and hormonal therapy and wished to continue on ustekinumab (8 weeks) due to its good effect on her UC. No other events, new signals or side effects were observed in our patients. Of those 5 patients who stopped ustekinumab, 2 underwent colectomy."[197] (emphasis in original)

216. The DDW Poster reports that among the 14 patients who continued to be observed there was a progressive drop in the median CAI, median CRP (C-Reactive protein) and median calprotein over a 3-, 6- and 9-month period.[198] I understand the reference to calprotein is a reference to fecal calprotein. My understanding is consistent with that of Professor Ciorba.[199]

217. The DDW Poster also reports:

> "Of all 19 patients:
> **- 37%** (7/19) were in remission at the start of the observation.

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[195] DDW Poster, last paragraph under the heading "Methods".
[196] Pavli #1 at [222].
[197] DDW Poster, first section under the heading "Results".
[198] DDW Poster, second section under the heading "Results".
[199] Ciorba at [165].

> - At 3, 6 and 9 months, clinical remission was observed in **79%** (15/19), **68%** (13/19) and **74%** (14/19) of patients, respectively.
> - At 3, 6 and 9 months all but one of these patients in remission were free of steroids, although 8 of them started with steroids.
>
> Of 12 patients with active disease at the start of the observation:
> - 5 patients achieved clinical remission at 1 month (**42%**), 10 patients at 3 months (**83%**), 9 patients at 6 months (**75%**) and 10 patients at 9 months (**83%**)."[200] (emphasis in original)

218. The conclusions drawn from the retrospective data analysis reported in the DDW Poster were that:

> "…ustekinumab was safe and effective as rescue medication in therapy-refractory or -intolerant ulcerative colitis. It seems possible that large ongoing trials confirm our findings and ustekinumab could become a new therapeutic option for ulcerative colitis."

Consideration

219. For the same reasons as I provided for Abstract P759, I consider that:

a. a skilled person would understand that the reference in the DDW Poster to the administration of "…*ustekinumab as approved for Crohn's disease* (6 mg/kg body weight as an infusion and 90 mg ustekinumab as s.c. injection every 8 weeks)…" is a reference to administration of Stelara® and with the IV and SC dosage regime as approved, by the relevant regulatory body, for CD;

b. off-label use of ustekinumab disclosed in the DDW Poster is a method of treatment that is relevant for the purposes of assessing novelty; and

c. the specific clinical endpoints of the claims of the opposed application are not features that can provide a meaningful difference over what was disclosed in the DDW Poster but are "merely supplementary information" about the measure of success which the method of administering ustekinumab is intended to achieve.[201]

220. Therefore, the same analyses I considered for Abstract P759 apply to the DDW Poster when assessing novelty. It follows that, for the same reasons as provided for Abstract P759, I conclude that claims 1-9, 17-28 and 30 lack novelty in view of the DDW Poster.

221. Additionally, I note that the DDW Poster reported that:

> "…median CRP dropped from 9 mg/L (range 1-33) to 5 mg/L (range 1-33) at 3 months, 2 mg/L (range 0-12) at 6 months and 2mg/L at 9 months (range 1-10).
>
> - Median calprotectin dropped from 428 ug/g (range 165-6000) to 236 ug/g (range 97-6000) at 3 months, 316 ug/g (range 84-3161) at 6 months and 260ug/g (range 63-1596) at 9 months."[202]

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[200] DDW Poster, third and fourth sections under the heading "Results".
[201] *Otsuka* at [321]-[322].
[202] DDW Poster, second section under the heading "Results".

222. That is, the DDW Poster discloses that at 3 months (week 12 after the first IV dose of ustekinumab) some patients demonstrated (a) fecal calprotein levels within a range 97-6000 µg/g, and (b) the median fecal calprotein is 236 µg/g. The opposed application describes the normalisation of fecal calprotein as being fecal calprotein concentration of ≤250 mg/kg. (the equivalent of ≤250 µg/g).[203] Therefore, I consider some patients of the study disclosed in the DDW Poster are subjects that have a normalisation of fecal calprotein by week 16 after the first IV dose of ustekinumab. While I note that Professor Ciorba stated that individual patient data were not reported (i.e., which patients had improvements in biomarker levels), I consider the limitations do not undermine the disclosure in the DDW Poster. [204] Consequently, I conclude that claim 26 lacks novelty in view of the DDW Poster.

223. In summary, I conclude that claims 1-9, 17-28 and 30 lack novelty in view of the DDW Poster. However, it has not been established that claims 10-16 and 29 lack novelty in view of the DDW Poster.

Abstract Tu1713

224. Abstract Tu1713 is an abstract for the DDW Poster. It was published by the AGA in association with the DDW conference, held in June 2018. Abstract Tu1713 is virtually identical to Abstract P759.[205]

225. Therefore, the same analyses I considered for Abstract P759 applies to Abstract Tu1713. It follows that, for the same reasons as provided for Abstract P759, I conclude that claims 1-9, 17-28 and 30 lack novelty in view of Abstract Tu1713. However, it has not been established that claims 10-16 and 29 lack novelty in view of Abstract Tu1713.

Conclusion on novelty

226. I conclude that claims 1-30 of the opposed application lack novelty in view of the cited prior art.

Inventive step

227. It is a requirement of subsection 18(1) of the *Act* that the invention, so far as claimed in any claim, involves an inventive step. Subsection 7(2) states:

> *For the purposes of this Act, an invention is to be taken to involve an inventive step when compared with the prior art base unless the invention would have been obvious to a person skilled in the relevant art in the light of the common general knowledge as it existed (whether in or out of the patent area) before the priority date of the relevant claim, whether that knowledge is considered separately or together with the information mentioned in subsection (3).*

228. Subsection 7(3) prescribes the information that may be considered as:

> *The information for the purposes of subsection (2) is:*
> *(a) any single piece of prior art information; or*

[203] The specification at page 67, lines 15-16.
[204] Ciorba at [165].
[205] Rohl #1 at [16], [18]-[20]; Pavli # 1 at [231], Ciorba at [155]-[156]

> *(b) a combination of any 2 or more pieces of prior art information that the skilled person mentioned in subsection (2) could, before the priority date of the relevant claim, be reasonably expected to have combined.*

229. The prior art base for the purposes of inventive step is made up of (1) information in a document that is publicly available anywhere, and (2) information that is made publicly available through doing an act anywhere.[206]

230. Once the CGK and relevant information have been identified, the test for whether an invention is obvious is to ask whether it would have been a matter of routine to proceed to the claimed invention. In *Wellcome Foundation Ltd v V.R. Laboratories (Aust.) Pty Ltd* Aickin J stated:

> "The test is whether the hypothetical addressee faced with the same problem would have taken as a matter of routine whatever steps might have led from the prior art to the invention, whether they be the steps of the inventor or not."[207]

231. Nicholas J provided a statement of principles relevant to assessing inventive step in *Hood v Bush Pharmacy Pty Ltd*:

> "Section 7(2) of the Act uses the word 'obvious' in the course of describing what must be established before an invention can be held not to involve an inventive step. Something may be 'obvious' in light of the common general knowledge, or the common general knowledge coupled with relevant s 7(3) information, if it is 'plain or open to the eye or mind, something which is perfectly evident to the person thinking on the subject' or something which 'would at once occur to anyone acquainted with the subject and desirous of accomplishing the end'
>
> An invention may also be obvious in light of the common general knowledge if the person skilled in the art faced with the same problem as the inventor would have taken as a matter of routine whatever steps might have led from the prior art to the invention, whether they be the steps of the inventor or not or (using the language of the 'modified Cripps question') if the person skilled in the art would be directly led as a matter of course to take such steps in the expectation that doing so might well produce a useful or better alternative to the prior art. However, a claimed invention is not obvious merely because the person skilled in the art would consider that it was 'worthwhile to try'."[208]

232. It is important to note the requirement for a reasonable expectation of success. This is explicit in the expectation that an approach "might well" succeed, and implicit in the characterisation of steps as those to be taken as a matter of routine.[209] However, success need not be guaranteed: "the relevant test is not knowing that steps will or would or even may well work, but merely expecting that the steps may well work."[210] Further, it is possible that the skilled person might be directly led to try more than one alternative expecting that each may well produce a useful or desired result.[211]

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[206] The *Act,* Schedule 1, definition of prior art base.
[207] [1981] HCA 12 at [45]; 148 CLR 262 at 286.
[208] [2020] FCA 1686; 158 IPR 229 at [116]-[117] (citations omitted).
[209] *Generic Health Pty Ltd v Bayer Pharma Aktiengesellschaft* [2014] FCAFC 73; 314 ALR 91 at [71].
[210] *Nichia Corporation v Arrow Electronics Australia Pty Ltd* [2019] FCAFC 2 ***(Nichia)***; 175 IPR 187 at [99].
[211] *Nichia* at [91]-[93].

233. Where an invention comprises a combination of integers, the question is whether the combination, not the individual integers, is obvious: "the selection of the integers out of 'perhaps many possibilities' … must be shown… to be obvious, bearing in mind that the selection of the integers in which the invention lies can be expected to be a process necessarily involving rejection of other possible integers".[212] As Aickin J said in the *3 M case*, "[t]he opening of a safe is easy when the combination has already been provided."[213]

Common general knowledge (CGK)

234. CGK is the background knowledge and experience available to all those working in the relevant art:

> "The notion of common general knowledge itself involves the use of that which is known or used by those in the relevant trade. It forms the background knowledge and experience which is available to all in the trade in considering the making of new products, or the making of improvements in old, and it must be treated as being used by an individual as a general body of knowledge."[214]

235. Professor Pavli and Professor Ciorba both set out what they believe to be the CGK regarding IBD, therapies for IBD and the clinical trial process in their declaration.[215] Having read the statement of the expert witnesses of both parties, I consider it is reasonable to conclude that there is general agreement between the experts that the following forms part of the CGK as of 24 September 2018:

a. CD and UC are the two main forms of IBD. In CD, inflammation can affect any part of the gastrointestinal tract, whereas in UC inflammation only affects the colon.[216]

b. While the practices for treating UC may have peculiarities in different jurisdictions, the general approach to treating UC included the use of 5-aminosalicylates (5-ASA), corticosteroids, immunomodulators (e.g., 6-mercaptopurine, azathioprine, methotrexate, or cyclosporine), biologic medicines that target specific inflammatory medicators of UC in the GI tract (e.g., infliximab, vedolizumab) and surgery. A combination of medications could be used, and the treatment depended on the severity of the condition as well as how a patient responded to one or more prescribed medications.[217] Infliximab (an anti-TNF-α agent) and vedolizumab (an $\alpha_4\beta_7$-integrin inhibitor) were biologic medicines used for a more targeted treatment of moderate to severe UC.[218] Surgery would be considered when all approved medication options had been exhausted or when a patient became refractory to one or more medications.[219]

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[212] *Aktiebolaget Hassle v Alphapharm Pty Ltd.* [2002] HCA 59 at [41] (***Aktiebolaget Hassle)***; 212 CLR 411 at 429 citing Aickin J in the ***3M case*** [1980] HCA 9 at [116]; 144 CLR 253 at 293.
[213] HCA 9 at [117]; 144 CLR 253 at 293.
[214] *Minnesota Mining and Manufacturing Co v Beiersdorf (Aust) Ltd* [1980] HCA 9 at [115]; 144 CLR 253 at page 292.
[215] Pavli#1 [71]-[162]; Ciorba [32]-[115].
[216] Pavli # 1 at [79], [81], [83]; Ciorba at [34]-[35], [38].
[217] Pavli #1 at [121]-[122]; Ciorba at [90]-[95], [188]-[189].
[218] Pavli #1 at [123]; Ciorba at [85], [91]-[94], [189].
[219] Pavli #1 at [126]; Pavli #2 at [45]; Ciorba at [96].

c. Several medications were approved by the Food and Drug Administration (FDA) in the USA at the priority date for treating UC and/or CD.[220] A table, from Professor Ciorba's evidence, with the US FDA approved medications is reproduced in Annex B of this decision. Professor Pavli prepared a similar table (also reproduced in Annex B of this decision) with all biologic medicines approved by the Therapeutic Goods Administration (TGA) in Australia.[221] From the tables, I note that the FDA and TGA had approved (1) infliximab, adalimumab and vedolizumab for the treatment of both CD and UC, and (2) ustekinumab (Stelara®) for the treatment of CD. While the FDA had approved tofacitinib for the treatment of UC before the priority date, the TGA had not.[222]

d. Human clinical trials can be divided into four phases. Phase I trials involve a small number of healthy people to evaluate safety. Phase II trials involve a larger number of patients to determine efficacy and appropriate dosing levels, as well as safety. Phase III trials, which form the basis for regulatory approval, involve an even larger number of patients to confirm efficacy and safety, including to gather information on potential adverse events not noticeable in the previously tested smaller and narrower patient population. Phase IV trials, conducted after regulatory approval has been obtained, involve monitoring efficacy and adverse events in a wider patient population over a longer period of time).[223]

e. Phase III clinical trials for ustekinumab in the treatment of UC were underway.[224]

f. The measure of success in a clinical trial is typically specified using one or more endpoints that are predetermined before commencing the trial to avoid the possibility of changing the endpoint to suit the data. The endpoints for clinical trials for CD or UC are typically clinical remission and/or clinical response measured in terms of one or more disease activity indices (**DAIs**).[225]

g. The most commonly used DAI for UC is the Mayo score (or full Mayo score), which involves providing a score from 0 to 3 for each of the following four domains over a seven-day period: stool frequency, rectal bleeding, mucosal appearance at endoscopy and a physician's global assessment (PGA), for a total score of 0 to 12. A score of ≤ 2 is considered remission, 3 to 5 is considered mildly active, 6 to 10 is considered moderately active and 11 or 12 is considered severely active. A modified version of the Mayo score which excludes the endoscopic assessment, and frequently used in clinical practice, is referred to as a partial Mayo score. Another modified version of the Mayo score which excludes the PGA, a subjective measure using the physician's assessment of disease activity and symptom activity, is referred to as the modified Mayo Score.[226]

h. Another DAI specific to UC is the Lichtiger index or modified Truelove and Witts colitis activity index (CAI). The Lichtiger index is based on clinical symptoms alone and is therefore more subjective.[227]

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[220] Ciorba at [75].
[221] Pavli #2 at [34].
[222] Pavli #1 at [135], [172]; Pavli #2 at [34], [39]; Ciorba at [75].
[223] Pavli #1 at [127]; Ciorba at [111].
[224] Pavli #1 at [135].
[225] Ciorba at [114].
[226] Ciorba at [64]; Pavli #1 at [91]-[95].
[227] Ciorba [67], [150].

i. In clinical trials, clinical remission is commonly defined as a Mayo score ≤ 2, with none of the individual subscores for each of the four domains exceeding 1. In the US, the Food and Drug Administration (FDA) recommends defining clinical remission in terms of the modified Mayo score, with an absolute stool number ≤ 3, a rectal bleeding subscore of 0 and an endoscopy subscore of 0 or 1.[228]

j. Clinical response is typically defined as a decrease from the baseline in the full Mayo score of at least 3 points and at least 30%, which must include a decrease in the score for rectal bleeding of at least one point, or an absolute score for rectal bleeding not exceeding 1.[229]

Obviousness in light of CGK alone

Hypothetical task

236. After the expert witnesses had set out what they considered to be the CGK, each were presented with a hypothetical task which required considering "some possibilities for an improvement in the existing state of things, whether by the solution of a problem or otherwise."[230]

237. Professor Pavli was asked to consider the following:

> "Maddocks asked me to assume that I was part of a notional research group as at 24 September 2018, including one or more additional experts having different roles (the **Group).** Maddocks also asked me to assume that the Group has been asked to propose a medication for the treatment or management of UC which would be a useful alternative to, or better than, the medications that were approved for use for the treatment and/or management of UC, based on information that I knew and accepted and regarded to be widely known and generally accepted by other gastroenterologists (whether in Australia or overseas) working in the field of the diagnosis, treatment and management of IBD before 24 September 2018 (the **Task**)."[231](emphasis in original)

238. Professor Pavli explained that as the gastroenterologist in the Group, his role in respect of the Task would have involved selecting which medication(s) to put forward and appropriate dose(s) or dosage regimen(s) for those medication(s).[232]

239. Professor Pavli explained that the response to the task which immediately would have sprung to mind is the use of ustekinumab, based on the facts that: (a) ustekinumab had been TGA approved (in February 2017) and PBS-listed (in September 2017) for use in the treatment of CD; (b) most medications which were indicated for the CD were also indicated for the treatment of UC; and (c) ustekinumab was the subject of the ongoing UNIFI Phase Ill clinical trial for the treatment of UC which had commenced in around 2015.[233] These matters alone, to Professor Pavli's mind, would have made ustekinumab the standout choice.[234]

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[228] Ciorba at [65], [140].
[229] Pavli #1 at [91].
[230] *AstraZeneca* at [524].
[231] Pavli #1 at [163].
[232] Pavli #1 at [165].
[233] Pavli #1 at [167].
[234] Pavli #1 at [168].

240. Professor Pavli explained that his involvement in the UNIFI trial, and his off-label experience with ustekinumab, before 24 September 2018 would have further cemented ustekinumab in his mind as the clear first choice in response to the task. Although he was blinded during the clinical trial, because of his clinical assessment of the patients participating in the trial, he had observed that a number of patients had improved during the trial and he believed that at least some of these patients must have responded to ustekinumab.[235]

241. Professor Ciorba was asked to consider the following:

> "..DCCL asked me to assume that as at the Relevant Date I was a member of a pharmaceutical research team (**Team**) seeking to develop a pharmaceutical product (being either an entirely new drug candidate or an existing drug or drug candidate) for the treatment of UC, which would be an improvement on, or useful alternative to, the products that were approved at that time for use for the treatment of UC, based on information that I knew and accepted and regarded to be widely known and generally accepted by other gastroenterologists working in the Field (**Hypothetical Task**)."[236] (emphasis in original)

242. In response to the task, Professor Ciorba had regard to the unmet needs associated with existing drug products, which included the efficacy ceiling, speed of onset of action, immunogenicity, oral administration and gut specificity.[237] Professor Ciorba described the three main classes of therapeutic targets being investigated at the priority date were (1) cytokine signalling molecules (e.g., JAKS), (2) mediators of leukocyte trafficking (e.g., integrins and their corresponding endothelial cell adhesion molecule receptors, and SIP modulators), and (3) pro-inflammatory cytokines.[238] Professor Ciorba was aware that while tofacitinib (a pan-JAK inhibitor that inhibits all JAK isoforms) had FDA approval for UC at the relevant date, there were concerns that the mechanism of action of pan-JAKS inhibitors might be overly broad and could give rise to off-target effects. However, he was aware that single-JAK inhibitors were being developed at the priority date and considered these to "have the potential to balance the benefits of blocking multiple cytokines against the possibility of off-target effects".[239] Professor Ciorba response to the hypothetical task was to recommend investigation of the development of single-JAK inhibitors as these would have the potential to address the unmet needs in the treatment of UC.[240]

243. The applicant submitted that Professor Pavli's approach to the hypothetical task was overly narrow and impermissibly led Professor Pavli towards the claimed invention. This was because Professor Pavli (1) selected from existing medications that were already available on the market for the purpose of off-label use in UC patients, (2) the medication had to already be available on the market in Australia, and (3) the medication had to already be undergoing clinical trials for UC.[241] The applicant further submitted that Professor Pavli appeared to have assumed the position of a gastroenterologist working in Australia who was tasked with an immediate need to treat an individual UC patient who had exhausted all approved treatment options. The applicant also alleged that Professor Pavli's involvement in the UNIFI trials and his off-label experience

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[235] Pavli #1 at [169].
[236] Ciorba at [116].
[237] Ciorba at [120]-[125].
[238] Ciorba at [126].
[239] Ciorba at [130].
[240] Ciorba at [135].
[241] The AS at [197].

with ustekinumab meant that his evidence was tainted by hindsight and the information available to Professor Pavli was not available to other gastroenterologists in the field and not part of the CGK.[242]

244. I observe that the only medications that had been approved for use in the treatment of CD or UC in Australia in the ten years or so before 24 September 2018 were biologic medicines, these being infliximab, adalimumab, golimumab, vedolizumab and ustekinumab (see the table from Professor Pavli's EIR, reproduced in Annex B of this decision).[243] I also observe that before 24 September 2018 the FDA had approved (1) certolizumab pegol and natalizumabmesal for the treatment of CD, and (2) tofacitnib for the treatment of UC.[244] I consider that it is reasonable that the CGK of the skilled person included knowledge of the drugs that had obtained regulatory approval for the treatment of CD and UC in Australia and at least the USA. Therefore, following Professor Pavli's rationale that most medications which were indicated for the treatment of CD were also indicated for the treatment of UC (and vice versa), I consider that there were at least four potential drug candidates – ustekinumab, tofacitnib, certolizumab pegol and natalizumabmesal – that the skilled person could reasonably have considered to be a potential drug candidate for the hypothetical task.[245]

245. Professor Pavli omitted references to tofacitnib, certolizumab pegol and natalizumabmesal because (a) these medications had been not approved by the TGA for the treatment of CD or UC, and (b) he could not prescribe these medications, even off-label.[246] However, I note that Professor Pavli did consider tofacitinib, which was TGA-approved for use in rheumatoid arthritis and was the subject of Phase III clinical trials for use in the treatment of UC before 24 September 2018. However, because tofacitnib had not been approved for the treatment of CD and Professor Pavli had some reservations about the use of JAK inhibitors, tofacitnib would have been a very distant second choice compared to ustekinumab.[247]

246. Even if Professor Pavli ruled out tofacitnib as a potential drug candidate for the hypothetical task, there remained three drug candidates – ustekinumab, certolizumab pegol and natalizumabmesal – which had obtained FDA approval for the treatment of CD that the skilled person could reasonably have considered to be a potential drug candidate for the hypothetical task. While it was reasonable for Professor Pavli to consider practices of gastroenterologists working in Australia, on the balance of probabilities I consider that the skilled person would still have included certolizumab pegol and natalizumabmesal in their consideration and it was not necessary to have limited the potential drug candidates to those that had already been approved by the TGA. This is because the CGK of the skilled person is not limited to the jurisdiction in which they practice. Additionally, Professor Pavli admitted that he was aware of, and had regard to, drug approvals by the FDA, and this information would have formed part of the CGK of the skilled person.[248]

247. In my view, the idiosyncrasies associated with Professor Pavli's experience as a practitioner in Australia led him to select ustekinumab and exclude other potential drug candidates for the

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[242] The AS at [198]-[199].
[243] Pavli #2 at [11], [34].
[244] Ciorba at [75].
[245] Pavli #1 at [99].
[246] Pavli # 2 at [36], [103(e)], [105]
[247] Pavli #1 at [172], [135(a)].
[248] Pavli # 1 at [149], [208]; Pavli # 2 at [103(e)].

hypothetical task. I consider Professor Pavli's approach was influenced by his personal attributes and this approach may not reflect that of the notional skilled person.

Off-label usage

248. Professor Pavli stated that while off-label use of a drug is possible it is neither a simple nor inexpensive process.[249] The process involved submissions of applications to the TGA and hospital pharmacy to support off-label use of a drug when all other medical options had been exhausted and the patients were being considered for major surgery. In support of these applications, Professor Pavli cited published reports of case studies regarding successful off-label use of medications for the indication he sought to treat.[250] Professor Pavli had prescribed ustekinumab off-label to 10 patients with either CD or UC before the priority date.[251]

249. I can accept that the off-label prescription of some medications for the treatment of CD or UC is a practice that is known and generally accepted by gastroenterlologists in Australia and overseas.[252] However, Professor Pavli's explanation of the off-label prescription of drugs indicates to me that off-label use of drugs like ustekinumab, for the treatment of UC, was not done as a matter of routine but in order to avoid surgery. Professor Ciorba described this as a "Hail Mary" attempt to save a patient from undergoing surgery and is not necessarily the most appropriate approach depending on the individual circumstances of the patient.[253] Additionally, I am not satisfied that Professor Pavli's off-label experience with ustekinumab would have been available to other gastroenterologists in the field at the priority date. Therefore, I consider Professor Pavli's off-label experience with ustekinumab is not part of the CGK and cannot be used to support his selection of only ustekinumab as a standout choice for the hypothetical task.

Clinical trials

250. Does the fact that ustekinumab was the subject of the UNIFI Phase III clinical trial for the treatment of UC support the selection of ustekinumab as a standout choice for the hypothetical task?

251. Professor Pavli stated that Phase III IBD clinical trials typically cost in the order of tens or hundreds of millions of dollars and were only embarked upon when the pharmaceutical company sponsoring then had a high expectation that the drug would be approved. However, he also stated that medications might not progress to regulatory approval for reasons including safety, efficacy relative to other drugs or other commercial reasons.[254]

252. Additionally, Professor Pavli explained that clinical trials for IBD often involved medications which had already been approved for other diseases.[255] This was because there are fewer patients with IBD compared with, for example, rheumatoid arthritis and there is generally a greater incentive for pharmaceutical companies to bring to market medications for treatment of diseases with larger patient populations. Furthermore, once a drug is approved for one indication, pharmaceutical companies have also considered the use of the medication with other diseases,

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[249] Pavli #1 at [36].
[250] Pavli #1 at [140]; Pavli # 2 at [47(b)].
[251] Pavli #1 at [162].
[252] Pavli # 2 at [8], [47(d)]; Ciorba at [101]
[253] Ciorba at [103], [105], [235].
[254] Pavli # 1 at [128]-[129].
[255] Pavli # 1 at [130].

especially for medications which are directed to an idiopathic inflammatory disorder (this being, inflammation for which there is no obvious infection as the cause) because there are features common to the inflammation arising from these disorders. He also stated that:

> "If a drug works for one of these idiopathic inflammatory diseases, then there is generally *a rational basis for an expectation that it would work (at least to some extent)* on another of these idiopathic inflammatory diseases. This is more so where there is a greater overlap between the relevant basic inflammation mechanisms, such as the involvement of TNF-α in inflammation in the joints and gut (i.e. infliximab) and the involvement of IL-23 in inflammation in the skin and gut (i.e. ustekinumab)."[256] (emphasis added)

253. From Professor Pavli's evidence, I understand that there are various reasons a pharmaceutical company might be motivated to select a drug for Phase III IBD clinical trials, some of which are commercial reasons. Therefore, I agree with the applicant that a skilled person cannot infer an expectation of success merely from the fact that a drug had progressed to a Phase III clinical trial.[257] I also note that Professor Pavli ruled out tofacitnib as a potential candidate for the hypothetical task even though tofacitnib had been approved by the FDA for the treatment of UC. Consequently, I am of the view that the mere fact that ustekinumab was the subject of UNIFI Phase III clinical trial for the treatment of UC does not support the opponent's case that ustekinumab was a standout choice for the hypothetical task.

254. I am cognisant of the statement of the Full Court in *Sandoz AG v Bayer Intellectual Property GmbH* that the risk of failure to gain regulatory approval is common in the field of drug development and establishes the baseline or context for the inventive step inquiry; it should not be determinative of the outcome.[258] However, the evidence in the present circumstances has required fine balancing and for the reasons already discussed, I consider Professor Pavli's exposure to ustekinumab is such that I cannot safely conclude that his evidence is indicative of the notional skilled person. Therefore, I attach limited weight to Professor Pavli's evidence regarding ustekinumab as the standout choice for the hypothetical task of assessing inventive step.

Conclusion on obviousness in light of CGK alone

255. I consider the opponent has not established that when considering the CGK alone, the PSA would be directly led as a matter of course to select only ustekinumab to treat moderately to severely active UC in the expectation that doing so might well produce a useful alternative to the prior art. Consequently, I conclude that the opponent has not established that any of the claims of the opposed application lacks an inventive step in light of CGK alone before the priority date of the claims.

Obviousness in light of citations considered together with CGK

256. The opponent relies on the following documents to allege lack of inventive step:

- CTR 236;
- Abstract P759

[256] Pavli # 1 at [131].
[257] The AS at [91], citing Ciorba at [191].
[258] [2024] FCAC135 at [92]; 183 IPR 309.

- DDW Poster; and
- Abstract Tu1713.[259]

Obviousness in light of CTR 236 considered together with common general knowledge

257. I have previously found that the disclosure of CTR 236 anticipates claims 1-3, 6-19 and 22-30 of the opposed application. Relevant for the present purposes, there is a clear teaching of a deliberate administration of ustekinumab for the intended purpose of treating moderately to severely active UC to achieve the intended results claimed in the claims. It follows from the discussion that each of claims 1-3, 6-19 and 22-30 lacks an inventive step in light of CTR 236 considered together with CGK.

Claims 4, 5, 20 and 21

258. CTR 236 does not disclose ustekinumab formulated with the claimed excipients. However, before 24 September 2018, it is a fact that Stelara® was the only ustekinumab formulation that had obtained regulatory approval and marketed by Janssen.[260] The Stelara® IV and SC formulations had the claimed excipients.[261] The question for the purpose of inventive step is whether it would have been a matter of routine for a skilled person to use Stelara® in the UNIFI Phase III clinical trials.

259. Professor Pavli stated that as a practical matter an antibody must be formulated to be administered to a patient (e.g., with other constituents put into a liquid formulation for IV infusion or SC injection). He also stated that given that Janssen was the sponsor of the UNIFI Phase III clinical trials, he understood the references to the administration of ustekinumab in CTR 236 to be references to the administration of Stelara®.[262]

260. I consider it is reasonable to infer from Professor Pavli's evidence that it would be a matter of routine for a skilled person to use Stelara® in the methods taught by CTR 236 since this was the only ustekinumab formulation which was approved for administration in humans at the priority date. Professor Pavli stated that gastroenterologists, including himself, would refer to Product Information documents or equivalent documents approved by the regulator of the relevant country (e.g., "Labels" approved by the FDA) for information regarding the medications. He further stated that if provided with any of CTR 236, Abstract P759, the DDW Poster and Abstract Tu1713, he would have read each of the documents together with the Stelara 2017 PI.[263] I understand Professor Pavli to mean that it was standard practice for a skilled person to combine the information in the Stelara 2017 PI, which included the IV and SC formulations, with the information disclosed in any one of the prior art citations.[264] Therefore, I consider that the skilled person, having led as a matter of routine to use Stelara® in the UNIFI Phase III clinical trials, would also arrive at method of administering ustekinumab with the excipients as claimed in each of claims 4, 5, 20 and 21. Consequently, I conclude that each of claims 4, 5, 20 and 21 lacks inventive step in light of CTR 236 considered together with CGK.

Conclusion on obviousness in light of CTR 236 considered together with CGK

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[259] The OS at [138]-[142].
[260] Pavli #1 at [186]; Pavli #2 at [34]; Ciorba at [75].
[261] Pavli # 1 at [288]-[291]; Kayser at [44]-[55].
[262] Pavli # 1 at [186].
[263] Pavli # 1 at [208], [234].
[264] The Stelara® IV and SC formulations are disclosed on pages 1-2 of the Stelara 2017 PI.

261. I conclude that each of claims 1-30 lacks inventive step in light of CTR 236 considered together with CGK.

Obviousness in light of Abstract P759 considered together with common general knowledge

262. I have previously found that the disclosure of Abstract P759 anticipates claims 1-9, 17-28 and 30. Relevant for the present purposes, there is a clear teaching of a deliberate administration of ustekinumab for the intended purpose of treating moderately to severely active UC to achieve the intended results claimed in the claims. It follows from the discussion that claims 1-9, 17-28 and 30 lack an inventive step in light of Abstract P759 considered together with the CGK.

Claims 10-16

263. I have previously found Abstract P759 to disclose that clinical remission was achieved in some patients by week 16 after the first IV dose of ustekinumab, but there is no disclosure that clinical remission continues at least 44 weeks after the first IV dose of ustekinumab.

264. Professor Pavli stated that he would have expected some participants treated with ustekinumab in accordance with the dosage regime set out in Abstract P759 to have achieved clinical remission by week 16 and continued to remain in clinical remission (1) until at least 44 weeks after the first IV induction dose of the ustekinumab, as well as (2) until at least 44 weeks after the first maintenance dose of ustekinumab (this being 52 weeks after the first IV induction dose of ustekinumab).[265]

265. Professor Ciorba stated that periods of remission amongst CD and UC patients can vary, lasting weeks, months or years. However, Professor Ciorba also stated that patients typically experience relapsing disease, which involves periods of active disease ("flares") alternating with periods of remission.[266]

266. The question for the purposes of inventive step is whether a skilled person would have as a matter of routine continued antibody treatment with an expectation that clinical remission would continue in some subjects, for at least 44 weeks after the first IV dose of antibody, in light of the disclosure in Abstract P759. I consider that it is reasonable to infer from the evidence of the expert witnesses that the answer is yes. Therefore, I conclude that each of claims 10-16 lacks an inventive step in light of Abstract P759 considered together with CGK.

Claim 29

267. Whilst Abstract P759 does not explicitly disclose a maintenance period of 44 weeks, the disclosure does not limit the number of repeats of the maintenance dose (this being 90 mg ustekinumab as a SC injection every 8 weeks). The median follow-up period was disclosed as 27 weeks with a range of 15-40 weeks. Therefore, I consider it is reasonable that the skilled person would understand that Abstract P759 teaches a maintenance period of various lengths. However, I consider the evidence does not establish that it would be a matter of routine for the skilled person to use a maintenance period of 44 weeks. Consequently, I conclude it has not been

[265] Pavli # 1 at [333], [335].
[266] Ciorba at [37], [40].

established that claim 29 lacks an inventive step in light of Abstract P759 considered together with CGK.

Conclusion on obviousness in light of Abstract P759 considered together with CGK

268. I conclude that each of claims 1-28 and 30 lacks inventive step in light of Abstract P759 considered together with CGK. However, it has not been established that claim 29 lacks an inventive step in light of Abstract P759 considered together with CGK.

Obviousness in light of DDW Poster considered together with common general knowledge

269. I have previously found that the disclosure of DDW Poster anticipates claims 1-9, 17-28 and 30 as there is a clear teaching of a deliberate administration of ustekinumab for the intended purpose of treating moderately to severely active UC to achieve the intended results claimed in these claims. It follows from the discussion that claims 1-9, 17-28 and 30 lack inventive step in light of the DDW Poster considered together with the CGK.

Claims 10-16 and 29

270. I have previously found that the disclosure of DDW Poster is very similar to that of Abstract P759. Therefore, the same analyses for assessing inventive step that I considered for Abstract P759 concerning claims 10-16 and 29 apply to the DDW Poster. It follows that, for the same reasons provided for Abstract P759, I conclude that each of claims 10-16 lacks inventive step in light of the DDW Poster considered together with the CGK. However, it has not been established that claim 29 lacks an inventive step in light of the DDW Poster considered together with the CGK.

Conclusion on obviousness in light of the DDW Poster considered together with CGK

271. I conclude that each of claims 1-28 and 30 lacks inventive step in light of the DDW Poster considered together with the CGK. However, it has not been established that claim 29 lacks an inventive step in light of the DDW Poster considered together with the CGK.

Obviousness in light of Abstract Tu1713 considered together with common general knowledge

272. Since the disclosure in Abstract Tu1713 is virtually identical to Abstract P759, the same analyses I considered for Abstract P759 applies to Abstract Tu1713. It follows that, for the same reasons as provided for Abstract P759, I conclude that claims 1-28 and 30 lack inventive step in light of Abstract Tu1713 considered together with CGK. However, it has not been established that claim 29 lacks an inventive step in light of the Abstract Tu1713 considered together with the CGK.

Conclusion on obviousness

273. I conclude that each of claims 1-30 of the opposed application lacks inventive step in light of cited prior art considered together with CGK.

Support

274. Section 40(3) of the *Act* requires that the claims must be supported by matter disclosed in the specification. Burley J considered the requirement of support in *Merck Sharp & Dohme Corporation v Wyeth LLC (No 3)* ***(Merck)*** and noted the claims will be appropriately supported if they "correspond to the technical contribution to the art".[267]

275. The technical contribution to the art is a subtle concept that is not to be confused with the inventive concept that is often discussed in relation to inventive step. The distinction was explained by Walker LJ in *Generics (UK) Limited v H Lundbeck A/S* [2009] UKHL 12 (***Generics UK(HL)***):

> "The expressions are certainly connected, but I do not think it is helpful (either in considering Lord Hoffmann's opinion, or generally) to treat them as having precisely the same meaning. 'Inventive concept' is concerned with the identification of the core (or kernel, or essence) of the invention – the idea or principle, of more or less general application (see *Kirin-Amgen* [2005] RPC 9 paras 112-113) which entitles the inventor's achievement to be called inventive. The invention's technical contribution to the art is concerned with the evaluation of its inventive concept – how far forward has it carried the state of the art? The inventive concept and the technical contribution may command equal respect but that will not always be the case."[268]

276. An important question will often be whether the technical contribution to the art is a general principle or the specific examples in the specification. Lord Hoffmann gave some examples in *Biogen v Medeva Plc [1997] RPC 1* ***(Biogen)***:

> "Thus if the patentee has hit upon a new product which has a beneficial effect but cannot demonstrate that there is a common principle by which that effect will be shared by other products of the same class, he will be entitled to a patent for that product but not for the class, even though some may subsequently turn out to have the same beneficial effect. On the other hand, if he has disclosed a beneficial property which is common to the class, he will be entitled to a patent for all products of that class (assuming them to be new) even though he has not himself made more than one or two of them."[269] [citations omitted]

277. In *Merck* Burley J referred to *CSR Building Products Limited v United States Gypsum Company* [2015] APO 72 ***(CSR)***, where the delegate adopted the summary provided by Aldous J in *Schering Biotech Corp's Application,* [1993] RPC 249 at 252-253, to answer the question of the claim support obligation:

> "… to decide whether the claims are supported by the description it is necessary to ascertain what is the invention which is specified in the claims and then compare that with the invention which has been described in the specification. Thereafter the court's task is to decide whether the invention in the claims is supported by the description. I do not believe that the mere mention in the specification of features appearing in the claim will necessarily be a sufficient support. The word 'support'

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[267] [2020] FCA 1477; 155 IPR 1 at [530]-[531] citing Walker LJ in *Generics UK(HL)* at 19 who referenced *Fuel Oils/EXXON* (T409/91) [1994] OJ EPO 653 (***Exxon***) at 659.
[268] *Generics UK(HL)* at [30].
[269] *Biogen* at 49.

> means more than that and requires the description to be the base which can fairly entitle the patentee to a monopoly of the width claimed."[270]

278. Burley J stated:

> "That approach encapsulates broadly the claim support obligation under s 40(3). To it may be added the requirement that the technical contribution to the art must be ascertained. Where it is a product, it is that which must be supported in the sense that the technical contribution to the art disclosed by the specification must justify the breath of the monopoly claimed."[271]

279. The considerations for the approach as stated in *CSR*, which the Federal Court have approved, are:

> "i) construe the claims to determine the scope of the invention as claimed,
> ii) construe the description to determine the technical contribution to the art, and
> iii) decide whether the claims are supported by the technical contribution to the art."[272]

The opponent's allegations

280. The opponent alleged that the claims of the opposed application include use of *any* anti-IL-12/IL-23p40 antibody having the same CDRs as ustekinumab to treat UC but the disclosure in the specification does not extend beyond ustekinumab. The opponent also alleged that the scope of the claims includes an antibody with an altered Fc region which can play a role in pharmacokinetics and bioavailability. Therefore, the opponent alleged that the work involved in identifying any other antibody which would work in the claimed method involves undue experimentation. Consequently, the opponent alleged that a claim to any other antibody, apart from ustekinumab, exceeds the technical contribution of the application and lacks support.[273]

281. The opponent's allegations rely on:

- Professor Pavli's understanding that claim 1 includes ustekinumab itself and also an antibody with the same variable regions as ustekinumab but with different constant regions as ustekinumab; [274] and
- Professor Ciorba's explanation of the typical structure of antibodies which included the following observations:

> "…Generally speaking, the amino acid sequence of the CDRs informs the binding specificity and affinity of the antibody molecule. The stem of the Y-shaped antibody structure is the Fragment Crystallizable (**Fc**) region, formed by the constant regions of the heavy chains, and is responsible for antibody effector function, as the region interacts with Fc receptors and complement proteins. The Fc region is typically not important for targeting and neutralising soluble antigens, including soluble inflammatory cytokines.

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[270] *Merck* at [546].
[271] *Merck* at [547].
[272] *CSR* at [115].
[273] The OS at [149]; the ORS at [39]-[40]; the OPHS at [26]-[30].
[274] Pavli # 1 at [282].

However, the Fc region can play a role in pharmacokinetics / bioavailability."[275] (bold font in original)

What is the technical contribution to the art?

282. While the examples in the opposed specification describe the use of ustekinumab to treat moderately to severely active UC, the specification also provides a general disclosure that antibodies with the same six CDRs as ustekinumab can be used to treat the condition. As previously discussed, the specification uses the term "anti-IL-12/IL-23p40 antibody" to refer to a monoclonal antibody (mAb) or antigen binding fragment thereof, that binds to the 40 kDa (p40) subunit shared by cytokines interleukin-12 and interleukin 23 (IL-12/23p40).[276] Ustekinumab (STELARA®) is an embodiment of such a mAb and prevents IL-12 and IL-23 bioactivity by inhibiting their interaction with the cell surface IL-12Rß1 receptor protein. Ustekinumab effectively neutralises IL-12 (Th1)- and IL-23 (Th17)-mediated cellular responses through this mechanism of action.[277]

283. I have also previously found that an antibody with the same six CDR sequences as ustekinumab would be expected to have the same binding specificity and affinity as ustekinumab. Furthermore, the specification states that the affinity of an antibody can be tested using methods that are known to the skilled person.[278] Therefore, I consider the technical contribution to the art is the use of an anti-IL-12/IL-23p40 antibody having the six defined CDRs sequences (these being amino acid sequences SEQ ID NO: 1 to SEQ ID NO: 6) to bind to the common p40 subunit of IL-12 and IL-23 and thereby neutralise the cellular responses mediated by these cytokines.

284. While the specification states that certain embodiments of the antibody comprise an altered (e.g. mutated) Fc region to reduce or enhance the effector function of the antibody, the specification also discloses that effector functions can be assessed using various assays, for example Fc binding assays, ADCC assays, CDC assays, etc.[279] I consider that a skilled person would understand the specification to teach that assays for testing effector functions are generally known and part of routine experimentation.

285. Therefore, while the inclusive nature of the term "comprising" means the claims can include an altered Fc region, I consider that the work involved in identifying an antibody with an altered Fc region which would work in the claimed method would be part of routine experimentation a skilled person can expect to perform.

286. I also note that apart from Professor Ciorba's statement regarding the role of the Fc region (which was made in the context of explaining the structure of an antibody), there is no evidence that there were in fact issues of pharmacokinetics and bioavailability which involve undue experimentation. Therefore, I consider the opponent has not discharged its burden of proof that the work involved in identifying whether any other antibody, apart from ustekinumab, would work in the claimed method involves undue experimentation.

Are the claims supported?

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[275] Ciorba at [74].
[276] The specification at page 10, lines 19-22.
[277] The specification at page 3, lines 7-12 and page 31, lines 16-18.
[278] The specification at page 25, lines 11-19.
[279] The specification at page 20, lines 17-23; page 21 lines 1-9.

287. I have previously interpreted the scope of independent claims 1, 17, 29 and 30 to include use of an antibody with the same six CDRs as ustekinumab, and ustekinumab itself, in a method of treating UC. Since the amino acid sequence of the CDRs informs the binding specificity and affinity of the antibody molecule, I consider the scope of claims 1, 17, 29 and 30 corresponds to the technical contribution to the art.

288. I also consider the scope of the appended claims 2-16 and 18-28 corresponds to the technical contribution to the art for similar reasons as discussed for the independent claims.

289. Consequently, I conclude that the opponent has not established that any of the claims lack support from the subject matter disclosed in the opposed application.

Conclusion

290. Each of claims 1-30 of the opposed application lacks novelty in view of the cited prior art. Each of claims 1-30 of the opposed application lacks inventive step in light of cited prior art considered together with CGK.

291. It has not been established that any of the claims lack support from the subject matter disclosed in the opposed application.

292. While not certain, it is possible that there is subject matter disclosed in the specification which could be used as a basis to amend the claims to overcome my findings. Consequently, Janssen Biotech, Inc. is given two months from the date of this decision to propose suitable amendments.

Costs

293. It is normal that costs should follow the event. I see no reason to depart from that result. Costs according to Schedule 8 are awarded against Janssen Biotech, Inc..

Dr A. Lim
Delegate of the Commissioner of Patents

Annex A: The claims of the opposed specification

1. A method of treating moderately to severely active ulcerative colitis (UC) in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising an effective amount of an anti-IL-12/IL-23p40 antibody, wherein the antibody comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region comprising: a complementarity determining region heavy chain 1 (CDRH1) amino acid sequence of SEQ ID NO:1; a CDRH2 amino acid sequence of SEQ ID NO:2; and a CDRH3 amino acid sequence of SEQ ID NO:3; and the light chain variable region comprising: a complementarity determining region light chain 1 (CDRL1) amino acid sequence of SEQ ID NO:4; a CDRL2 amino acid sequence of SEQ ID NO:5; and a CDRL3 amino acid sequence of SEQ ID NO:6, wherein after treating with the antibody, the subject is a responder to treatment by at least one measure of response to treatment selected from the group consisting of: (i) clinical remission based on at least one of the global definition of clinical remission with Mayo score ≤ 2 points with no individual subscore > 1 and the US definition of clinical remission with absolute stool number ≤ 3, rectal bleeding subscore of 0 and Mayo endoscopy subscore of 0 or 1, (ii) endoscopic healing with a Mayo endoscopy subscore of 0 or 1, (iii) clinical response based on the Mayo endoscopy subscore, (iv) mucosal healing, and (v) clinical response as determined by a decrease from baseline in the Mayo score by ≥30% and ≥3 points and a decrease from baseline in the rectal bleeding subscore ≥1 points or a rectal bleeding subscore of 0 or 1.

2. The method of claim 1, wherein the antibody comprises the heavy chain variable region of the amino acid sequence of SEQ ID NO:7 and the light chain variable region of the amino acid sequence of SEQ ID NO:8.

3. The method of claim 1, wherein the antibody comprises a heavy chain of the amino acid sequence of SEQ ID NO:10 and a light chain of the amino acid sequence of SEQ ID NO:11.

4. The method of any one of claims 1-3, wherein the antibody is in a pharmaceutical composition for intravenous administration comprising a solution comprising 10 mM L-histidine, 8.5% (w/v) sucrose, 0.04% (w/v) polysorbate 80, 0.4 mg/mL Lmethionine, and 20 µg/mL EDTA disodium salt, dehydrate, at pH 6.0.

5. The method of any one of claims 1-3, wherein the antibody is in a pharmaceutical composition for subcutaneous administration comprising a solution comprising 6.7 mM L-histidine, 7.6% (w/v) sucrose, 0.004% (w/v) polysorbate 80, at pH 6.0.

6. The method of claim 4, wherein the antibody is administered intravenously to the subject at week 0 of the treatment, at a dosage of about 6.0 mg/kg body weight of the subject or 130 mg, 260 mg, 390 mg or 520 mg per administration.

7. The method of claim 6, wherein the antibody is further administered subcutaneously to the subject at week 8 of the treatment, at a dosage of about 90 mg per administration.

8. The method of claim 7, wherein the subject had previously failed or was intolerant of at least one therapy selected from the group consisting of an anti-TNF, vedolizumab, corticosteroids, azathioprine (AZA), and 6 mercaptopurine (6 MP), or the subject had demonstrated corticosteroid dependence.

9. The method of claim 7, wherein the antibody is administered in a maintenance dose every 8 weeks after the treatment at week 8 or every 12 weeks after the treatment at week 8.

10. The method of claim 9, wherein the subject is identified as having a clinical remission based on at least one of the global definition and the US definition by week 16 of the treatment and the clinical remission continues at least 44 weeks after week 0.

11. The method of claim 9, wherein the subject is in corticosteroid-free clinical remission at least 44 weeks after week 0.

12. The method of claim 9, wherein the subject is identified as having an endoscopic healing continuing at least 44 weeks after week 0.

13. The method of claim 9, wherein the subject is identified as achieving a clinical response based on the Mayo endoscopy subscore continuing at least 44 weeks after week 0.

14. The method of claim 9, wherein the subject is identified as having a mucosal healing continuing at least 44 weeks after week 0.

15. The method of claim 9, wherein the subject is identified as having a normalization of one or more biomarkers selected from the group consisting of C-reactive protein, fecal lactoferrin and fecal calprotectin continuing at least 44 weeks after week 0.

16. The method of claim 9, wherein the subject is in clinical response as determined by a decrease from baseline in the Mayo score by ≥30% and ≥3 points and a decrease from baseline in the rectal bleeding subscore ≥1 points or a rectal bleeding subscore of 0 or 1 continuing at least 44 weeks after week 0.

17. A method of treating moderately to severely active ulcerative colitis (UC) in a subject in need thereof, comprising:

a. intravenously administering to the subject an anti-IL-12/IL-23p40 antibody in a first pharmaceutical composition at a dosage of about 6.0 mg/kg body weight of the subject or 130 mg, 260 mg, 390 mg or 520 mg per administration at week 0 of the treatment, and

b. subcutaneously administering to the subject the anti-IL-12/IL-23p40 antibody in a second pharmaceutical composition at a dosage of 90 mg per administration at week 8 of the treatment,

wherein the antibody comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region comprising: a complementarity determining region heavy chain 1 (CDRH1) amino acid sequence of SEQ ID NO:1; a CDRH2 amino acid sequence of SEQ ID NO:2; and a CDRH3 amino acid sequence of SEQ ID NO:3; and the light chain variable region comprising: a complementarity determining region light chain 1 (CDRL1) amino acid sequence of SEQ ID NO:4; a CDRL2 amino acid sequence of SEQ ID NO:5; and a CDRL3 amino acid sequence of SEQ ID NO:6; and

wherein the subject is a responder to treatment by at least one measure of response to treatment selected from the group consisting of: (i) having a clinical remission based on at least one of the global definition of clinical remission with Mayo score ≤ 2 points with no individual

subscore > 1 and the US definition of clinical remission with absolute stool number ≤ 3, rectal bleeding subscore of 0 and Mayo endoscopy subscore of 0 or 1, (ii) having an endoscopic healing with a Mayo endoscopy subscore of 0 or 1, (iii) achieving a clinical response based on the Mayo endoscopy subscore, (iv) having a mucosal healing, and (v) in clinical response as determined by a decrease from baseline in the Mayo score by ≥30% and ≥3 points and a decrease from baseline in the rectal bleeding subscore ≥1 points or a rectal bleeding subscore of 0 or 1, and

wherein the subject had previously failed or was intolerant of at least one therapy selected from the group consisting of: an anti-TNF, vedolizumab, corticosteroids, azathioprine (AZA), and 6 mercaptopurine (6 MP), or the subject had demonstrated corticosteroid dependence.

18. The method of claim 17, wherein the antibody comprises the heavy chain variable region of the amino acid sequence of SEQ ID NO:7 and the light chain variable region of the amino acid sequence of SEQ ID NO:8.

19. The method of claim 17, wherein the antibody comprises a heavy chain of the amino acid sequence of SEQ ID NO:10 and a light chain of the amino acid sequence of SEQ ID NO:11.

20. The method of any one of claims 17-19, wherein the first pharmaceutical composition further comprises a solution comprising 10 mM L-histidine, 8.5% (w/v) sucrose, 0.04% (w/v) polysorbate 80, 0.4 mg/mL L-methionine, and 20 μg/mL EDTA disodium salt, dehydrate, at pH 6.0.

21. The method of claim 20, wherein the second pharmaceutical composition further comprises a solution comprising 6.7 mM L-histidine, 7.6% (w/v) sucrose, 0.004% (w/v) polysorbate 80, at pH 6.0.

22. The method of any one of claims 17-19, wherein the subject is identified as having a clinical remission based on at least one of the global definition and the US definition by week 16 of the treatment.

23. The method of any one of claims 17-19, wherein the subject is identified as having an endoscopic healing by week 16 of the treatment.

24. The method of any one of claims 17-19, wherein the subject is identified as achieving a clinical response based on the Mayo endoscopy subscore by week 16 of the treatment.

25. The method of any one of claims 17-19, wherein the subject is identified as having a mucosal healing by week 16 of the treatment.

26. The method of any one of claims 17-19, wherein the subject is identified as having a normalization of one or more biomarkers selected from the group consisting of C-reactive protein, fecal lactoferrin and fecal calprotectin by week 16 of the treatment.

27. The method of any one of claims 17-19, wherein the subject is in clinical response as determined by a decrease from baseline in the Mayo score by ≥30% and ≥3 points and a decrease from baseline in the rectal bleeding subscore ≥1 points or a rectal bleeding subscore of 0 or 1 by week 16 of the treatment.

28. The method of any one of claims 17-19, wherein the subject is not a responder to the treatment with the antibody by week 8 and is a responder to the treatment by week 16 of the treatment.

29. A method of treating moderately to severely active ulcerative colitis (UC) in a subject in need thereof, comprising:

a. intravenously administering to the subject an anti-IL-12/IL-23p40 antibody in a first pharmaceutical composition at a dosage of about 6.0 mg/kg body weight of the subject or 130 mg, 260 mg, 390 mg or 520 mg per administration at week 0 of the treatment, and

b. subcutaneously administering to the subject the anti-IL-12/IL-23p40 antibody in a second pharmaceutical composition at a dosage of 90 mg per administration at week 8 of the treatment,

wherein the antibody comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region comprising: a complementarity determining region heavy chain 1 (CDRH1) amino acid sequence of SEQ ID NO:1; a CDRH2 amino acid sequence of SEQ ID NO:2; and a CDRH3 amino acid sequence of SEQ ID NO:3; and the light chain variable region comprising: a complementarity determining region light chain 1 (CDRL1) amino acid sequence of SEQ ID NO:4; a CDRL2 amino acid sequence of SEQ ID NO:5; and a CDRL3 amino acid sequence of SEQ ID NO:6, followed by a maintenance therapy,

wherein the maintenance therapy comprises subcutaneously administering to the subject the anti-IL-12/IL-23p40 antibody at a dosage of 90 mg per administration, once every 8 weeks or once every 12 weeks, and wherein the maintenance therapy is provided for 44 weeks and after treating with the antibody, the subject is a responder to treatment by at least one measure of response to treatment selected from the group consisting of: (i) having a clinical remission based on at least one of the global definition of clinical remission with Mayo score ≤ 2 points with no individual subscore > 1 and the US definition of clinical remission with absolute stool number ≤ 3, rectal bleeding subscore of 0 and Mayo endoscopy subscore of 0 or 1, (ii) having an endoscopic healing with a Mayo endoscopy subscore of 0 or 1, (iii) achieving a clinical response based on the Mayo endoscopy subscore, (iv) having a mucosal healing, and (v) in clinical response as determined by a decrease from baseline in the Mayo score by $\geq 30\%$ and ≥ 3 points and a decrease from baseline in the rectal bleeding subscore ≥ 1 points or a rectal bleeding subscore of 0 or 1.

30. A method of treating moderately to severely active ulcerative colitis (UC) in a subject in need thereof, comprising:

a. intravenously administering to the subject an anti-IL-12/IL-23p40 antibody comprising a heavy chain variable region of the amino acid sequence of SEQ ID NO:7 and a light chain variable region of the amino acid sequence of SEQ ID NO:8, in a first pharmaceutical composition at a dosage of about 6.0 mg/kg body weight of the subject or 130 mg, 260 mg, 390 mg or 520 mg per administration at week 0 of the treatment, and

b. subcutaneously administering to the subject the anti-IL-12/IL-23p40 antibody in a second pharmaceutical composition at a dosage of 90 mg per administration at week 8 of the treatment, followed by a maintenance therapy,

wherein the maintenance therapy comprises subcutaneously administering to the subject the anti-IL-12/IL-23p40 antibody at a dosage of 90 mg per administration, once every 8 weeks or once every 12 weeks, and after treating with the antibody, the subject is a responder to treatment by at least one measure of response to treatment selected from the group consisting of: (i) having a clinical remission based on at least one of the global definition of clinical remission with Mayo score ≤ 2 points with no individual subscore > 1 and the US definition of clinical remission with absolute stoolnumber ≤ 3, rectal bleeding subscore of 0 and Mayo endoscopy subscore of 0 or 1, (ii) having an endoscopic healing with a Mayo endoscopy subscore of 0 or 1, (iii) achieving a clinical response based on the Mayo endoscopy subscore, (iv) having a mucosal healing, (v) in clinical response as determined by a decrease from baseline in the Mayo score by ≥30% and ≥3 points and a decrease from baseline in the rectal bleeding subscore ≥1 points or a rectal bleeding subscore of 0 or 1.

Annex B:

Table reproduced from Professor Ciorba's EIA at [75] showing medications approved by the FDA for treating either CD or UC, or both, before 24 September 2018. The green cells indicate the FDA approval date for the relevant indication. The yellow cells indicate that the drug was either in ongoing clinical trials or no clinical trials were conducted in relation to the relevant indication. The red cells indicate a lack of safety and/or efficacy in the relevant indication.

Drug	Brand name	Class	FDA Approval date	
			CD	UC
Mesalamine	Lialda®	5-ASA	x	2007
Infliximab	Remicade®	Cytokine inhibitor (TNF-α)	1998	2005
Adalimumab	Humira®		2007	2012
Certolizumab pegol	Cimzia®		2008	-
Golimumab	Simponi®		Phase II*	2013
Natalizumabmesal	Tysabri®	Integrin inhibitor	2008	x
Vedolizumab	Entyvio®		2014	2014
Ustekinumab	Stelara®	Cytokine inhibitor (IL-12/IL-23)	2016	Phase III
Tofacitinib	Xeljanz®	JAK inhibitor	x	2018

* in combination with guselkumab

Table reproduced from Professor Pavli's EIR at [34] showing biologic medications approved by the TGA for the treatment of CD or UC, or both, before 24 September 2018.

Biologic medicine	Class	TGA approval year		Comments
		Crohn's disease	*UC*	
infliximab (REMICADE)	anti-TNF-α	2003	2007	
adalimumab (HUMIRA)		2007	2013	
golimumab (SIMPONI)		-	2014	
vedolizumab (ENTYVIO)	anti-$\alpha_4\beta_7$ integrin	2014	2014	
ustekinumab (STELARA)	anti-IL-12/IL-23	2017	-	In Phase III clinical trials for UC