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Paper 21
Date: October 17, 2024

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SHANGHAI HONGENE BIOTECH CORP.,
Petitioner,

v.

CHEMGENES CORP.,
Patent Owner.

IPR2023-00862
Patent 8,541,569 B2

Before JOHN G. NEW, ZHENYU YANG, and CYNTHIA M. HARDMAN, *Administrative Patent Judges.*

YANG, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Determining All Challenged Claims Unpatentable
35 U.S.C. § 318(a)

Granting Petitioner's Motion to Seal (Paper 19)
37 C.F.R. §§ 42.14, 42.54

I. INTRODUCTION

Shanghai Hongene Biotech Corp. ("Petitioner") filed a Petition (Paper 1, "Pet.") seeking *inter partes* review of claims 1 and 2 of U.S. Patent No. 8,541,569 B2 (Ex. 1001, "the '569 patent"). ChemGenes Corp. ("Patent Owner") did not file a Preliminary Response. We instituted trial to review the challenged claims. Paper 6.

After institution, Patent Owner filed a Response (Paper 10, "PO Resp.") and a Motion to Amend Claims (Paper 11, "MTA"). In the MTA, Patent Owner proposed to replace claims 1 and 2 with substitute claims 33 and 34. MTA 1–2. Petitioner filed an Opposition to Patent Owner's MTA (Paper 13) and a Reply to Patent Owner's Response (Paper 14, "Reply").

After we entered Preliminary Guidance on Patent Owner's Motion to Amend (Paper 15), Patent Owner requested authorization to withdraw its MTA (Ex. 3003). We granted that request. Paper 17. Thereafter, Patent Owner filed a Sur-reply to Petitioner's Reply (Paper 20, "Sur-reply").[1]

The Board has jurisdiction under 35 U.S.C. § 6 and issues this Final Written Decision pursuant to 35 U.S.C. § 318 and 37 C.F.R. § 42.73. For the reasons provided below, we find Petitioner has shown, by a preponderance of the evidence, the unpatentability of claims 1 and 2.

A. Related Matters

According to the parties, Patent Owner asserted the '569 patent against Petitioner in Case No. 1-22-cv-10290 (D. Mass.) but later voluntarily dismissed the district court action. Pet. vi; Paper 4, 2.

[1] Paper 20 is a redacted version of the Sur-reply. Patent Owner originally filed the Sur-reply under seal. *See* Paper 18.

Petitioner also filed IPR2023-00490 and IPR2023-00875, challenging two other patents asserted in the district court action. Paper 4, 2. In IPR2023-00490, we determined that claims 1–5 of U.S. Patent 9,884,885 were unpatentable. IPR2023-00490, Paper 35. In a concurrently entered decision, we determine that claims 1 and 2 of U.S. Patent 8,309,707 are unpatentable. IPR2023-00862, Paper 21.

B. The '569 Patent

The '569 patent "provides building blocks and methods for synthesizing very pure RNA in a form that can efficiently be modified at the 3′ end." Ex. 1001, Abstract.

The '569 patent explains that, at the time of its alleged invention, defined sequence RNA synthesis in the 3′→5′ direction was well established. *Id.* at 1:20–50. If the synthesized RNA requires a modification or labeling of the 3′-end, however, the 3′→5′ synthesis methodology is "challenging, difficult to synthesize and generally result[s] in low coupling efficiency and lower purity of the final oligonucleotide." *Id.* at 1:51–57. According to the '569 patent, "new synthetic methodologies are needed to synthesize RNA molecules quickly, and cleanly and in a form that allows for modification at the 3′ end." *Id.* at 1:58–60.

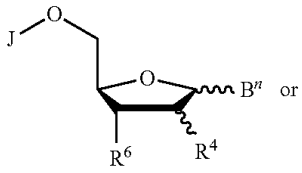
The '569 patent discloses reverse RNA monomer phosphoramidites for RNA synthesis in 5′→3′ direction, which leads to "very clean oligo synthesis that allows for the introduction of various modifications at the 3′ end cleanly and efficiently." *Id.* at 1:66–2:3.

C. Illustrative Claim

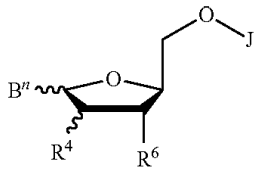
Claim 1 is illustrative of the claimed subject matter. We reproduce below only those parts relevant to our present analysis.

1. A compound of Formula Ia or Ib:

(Ia)



(Ib)



or a salt thereof, wherein:

J is H . . .;

. . .

R^4 is a -halo . . .;

. . .

R^6 is —H or —O—Z;

. . .

B^n is hydrogen or an optionally substituted nucleobase optionally functionalized at each exocyclic amine with an amine protecting group, wherein the nucleobase is selected from: . . . thymine, . . . 5-methylcytosine. . .

. . . .

Ex. 1001, 111:22–114:33.

D. Instituted Challenges to Patentability

We instituted trial to determine whether the challenged claims are unpatentable based on the following grounds:

Claim Challenged	35 U.S.C. §	Reference(s)/Basis
1	102(b)	Aerschot[2]

[2] Aerschot et. al., 3′-Fluoro-2′,3′-dideoxy-5-chlorouridine: Most Selective Anti-HIV1 Agent among a Series of New 2′- and 3′-Fluorinated 2′,3′-Dideoxynucleoside Analogues, 32 J. MED. CHEM. 1742–49 (1989) (Ex. 1004, "Aerschot").

Claim Challenged	35 U.S.C. §	Reference(s)/Basis
2	102(b)	Aerschot

Petitioner relies on the declaration of Phil S. Baran, Ph.D., as support for its Petition. Ex. 1003. Patent Owner relies on the Declaration of Patrick J. Hrdlicka, Ph.D., to support the Patent Owner Response. Ex. 2001.

II. ANALYSIS

A. Principles of Law

To prevail in this *inter partes* review, Petitioner "shall have the burden of proving a proposition of unpatentability by a preponderance of the evidence." 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d).

To show anticipation under 35 U.S.C. § 102, each and every claim element, arranged as in the claim, must be disclosed in a single piece of prior art. *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359 (Fed. Cir. 2008). For a claim directed to a genus, if a prior art reference discloses a species falling within the claimed genus, the species anticipates the genus. *In re Slayter*, 276 F.2d 408, 411 (CCPA 1960); *see also Fresenius USA, Inc. v. Baxter Int'l, Inc.*, 582 F.3d 1288, 1298 (Fed. Cir. 2009) (stating that when a claim element is written in Markush form, "the entire element is disclosed by the prior art if one alternative in the Markush group is in the prior art").

We analyze the instituted grounds of unpatentability in accordance with these principles.

B. Claim Construction

In an *inter partes* review, we construe a claim term "using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. [§] 282(b)." 37 C.F.R. § 42.100(b) (2020). Under that standard, the words of a claim "are generally given their ordinary

and customary meaning," which is "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc).

Claim terms need only be construed to the extent necessary to resolve the controversy. *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011). On this record and for purposes of this Decision, we see no need to address the construction of any claim term.

C. Level of Ordinary Skill in the Art

Petitioner contends that, as of the earliest possible priority date of the '569 patent,

> a person of ordinary skill in the art ("POSA") would have had a Ph.D. (or equivalent degree) in organic or medicinal chemistry, and 2-3 years of post-graduate work experience in medicinal chemistry, synthetic organic chemistry, and nucleic acid chemistry, including the development of oligonucleotide therapeutics, diagnostics, or building blocks.

Pet. 12 (citing Ex. 1003 ¶¶ 18–21).

Alternatively, Petitioner proposes that an individual holding a Bachelor's or Master's degree in organic chemistry or medicinal chemistry, "who had at least three years of work experience in these fields, and who had gained a thorough understanding of the development of nucleic acid-based materials, would also have qualified as a POSA." *Id.*

Patent Owner argues that a POSA would have had a Ph.D. (or equivalent degree) in organic chemistry, who, either during his or her Ph.D. studies, focused on, or has at least two to three years of post-graduate work experience in, "the development and syntheses of nucleosides, nucleotides, and nucleic acids, including, but not limited to, the syntheses of

oligonucleotides through solid phase oligonucleotide synthesis ('SPOS') pursuant to P(III) chemistry." PO Resp. 20–21. Alternatively, Patent Owner proposes that someone with a lesser degree but more (at least five years) extensive work experience in these fields would also have qualified as a POSA. *Id.* at 21.

The parties' proposed definitions of the level of ordinary skill, although different facially, are similar substantively. For example, both parties argue that a POSA would have high levels of skill, with advanced degrees and/or extensive work experience in organic chemistry.[3] *See* Pet. 12; PO Resp. 20–21. In addition, Petitioner contends that a POSA would have had experience in the development of oligonucleotide building blocks. Pet. 16. Similarly, Patent Owner asserts that a POSA would have had education and/or experience in "the development and syntheses of nucleosides, nucleotides, and nucleic acids." PO Resp. 20–21.

After considering the parties' arguments and the prior art, we determine that a POSA would have had a Ph.D. (or equivalent degree) in organic chemistry or medicinal chemistry, with at least two to three years of post-graduate work experience in the development and syntheses of nucleosides, nucleotides, and nucleic acids, including, but not limited to, the syntheses of oligonucleotides through solid phase oligonucleotide synthesis. In addition, an individual with a Bachelor's or Master's degree and at least five years of work experience in these fields also would qualify as a POSA.

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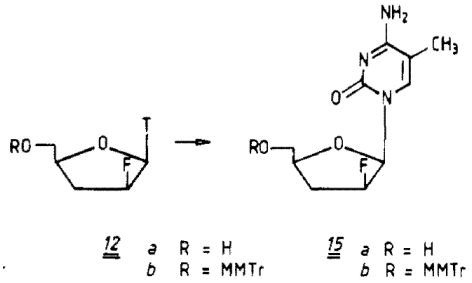
[3] Although Patent Owner proposes deleting "medicinal" chemistry from Petitioner's definition, it states that "would not exclude medicinal or other chemists so long as the chemist in question met the [other] requirements." PO Resp. 21 (citing Ex. 2001 ¶ 65).

Patent Owner contends that Petitioner's declarant, Dr. Baran, does not have significant background in P(III) chemistry. *Id.* at 18–19; Sur-reply 12–13. According to Patent Owner, Dr. Baran published only about a dozen papers that relate to oligonucleotide synthesis, and the focus of those papers appears to be on P(V) chemistry, which is fundamentally different from P(III) chemistry. PO Resp. 18–19; Sur-reply 12–13. Although it does not challenge Dr. Baran's qualification to provide opinion in this proceeding, Patent Owner asserts that "Dr. Baran's lack of experience in P(III) synthesis[] should be strongly considered" in our evaluation of the weight of Dr. Baran's testimony. Sur-reply 13.

Patent Owner's argument that Dr. Baran is principally experienced in P(V) chemistry presupposes that experience indicates an ignorance of P(III) chemistry. We do not find this position consistent with the breadth of Dr. Baran's experience as indicated by his Curriculum Vitae. *See* Ex. 1003, 47–102. We weigh the testimonies of both Dr. Baran and Dr. Hrdlicka, against the cumulative weight of the evidence of record in assessing their credibility and probative value.

D. Disclosure of Aerschot

Aerschot discloses the synthesis of a series of 2′- and 3′-fluorinated 2′,3′-dideoxynucleosides and 3′-azido-2′,3′-dideoxynucleosides. Ex. 1004, 1743. Specifically, it discloses compounds 12a and 15a as follows:



12 a R = H
b R = MMTr

15 a R = H
b R = MMTr

The figure above shows the chemical structures of compounds 12 and 15. *Id.* at 1744. Aerschot explains that compound 12a is 1-(2-Fluoro-2,3-dideoxy-(β-D-*threo*-pentofuranosyl)thymine and 15a is 1-(2-Fluoro-2,3-dideoxy-(β-D-*threo*-pentofuranosyl)-5-methylcytidine. *Id.* at 1745, 1747.

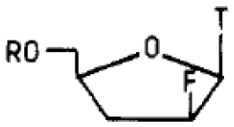
E. Alleged Anticipation of Claim 1

Petitioner asserts that Aerschot anticipates claim 1. Pet. 12–26. After reviewing the entire record developed at trial, and as explained below, we determine that Petitioner has shown, by a preponderance of the evidence, that Aerschot anticipates claim 1.

Claim 1 is directed to a genus of compounds having Formula Ia or Ib. It recites groups J, R^4, R^6, B^n, each as a Markush group. Petitioner argues that "[o]ne compound that falls within the scope of Claim 1 is Formula Ia in which J is H (hydrogen), R^4 is the -halo atom fluorine, R^6 is —H (hydrogen), and B^n is thymine ('T')." Pet. 16 (citing Ex. 1003 ¶¶ 81–83, 85). This thymine compound, according to Petitioner, has four different potential stereoisomeric configurations. *Id.* at 17–18 (citing Ex. 1003 ¶¶ 86–87). One configuration, Isomer A, has both fluorine and thymine "up," as relative to the plane of the ring structure. *Id.*

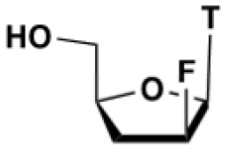
Petitioner asserts that Aerschot discloses Isomer A of claim 1 as compound 12a. *Id.* at 19 (citing Ex. 1003 ¶¶ 88–92). Petitioner provides the following comparison:

Aerschot compound 12a:



12 a R = H
b R = MMTr

Isomer A Species of Claim 1



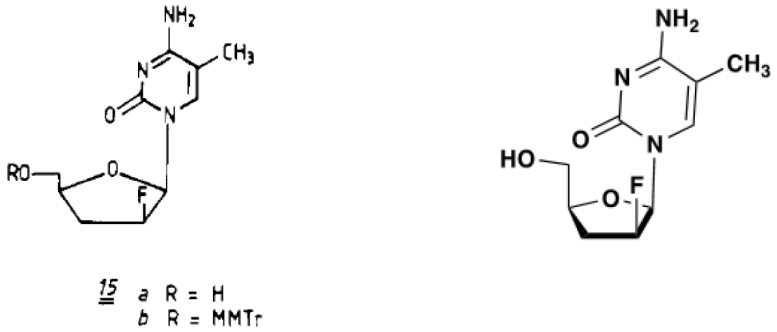
The figure above shows Petitioner's depiction of the side-by-side comparison of Aerschot compound 12a with Isomer A of claim 1. *Id.* (citing Ex. 1003 ¶¶ 87–88; Ex. 1004, 1744). Petitioner argues that these compounds are identical. *Id.* (citing Ex. 1003 ¶¶ 87–92; Ex. 1004, 1745, 1747).

Petitioner asserts that "[a]nother species of claim 1 is the compound of Formula Ia wherein J is H, R^4 is the -halo fluorine, R^6 is —H, and B^n is 5-methylcytosine." *Id.* at 22 (citing Ex. 1003 ¶ 106).
This 5-methylcytosine compound, according to Petitioner, also has four different potential stereoisomeric configurations.[4] *Id.* at 22–23 (citing Ex. 1003 ¶ 107). One configuration, Isomer A1, has both fluorine and 5-methylcytosine "up," as relative to the plane of the ring structure. *Id.*

Petitioner asserts that Aerschot discloses Isomer A1 of claim 1 as compound 15a. *Id.* at 23 (citing Ex. 1003 ¶ 108; Ex. 1004, 1744). Petitioner provides the following comparison:

[4] Petitioner argues, and Patent Owner does not dispute, that the only difference between the 5-methylcytosine compound and the thymine compound is the B^n group: in the former, it is 5-methylcytosine, whereas in the latter, it is thymine. Pet. 22 (citing Ex. 1003 ¶ 106 n.3).

Aerschot Compound 15a **Isomer A1 of Claim 1**



The figure above shows Petitioner's depiction of the side-by-side comparison of Aerschot compound 15a with Isomer A1 of claim 1. *Id.* (citing Ex. 1003 ¶¶ 107–108). Petitioner argues that these compounds are chemically identical.[5] *Id.*

Patent Owner does not dispute Petitioner's anticipation challenge of claim 1. *See* PO Resp. 24–25; Sur-reply 14. Instead, Patent Owner contends that the challenge to claim 1 is moot subject to the MTA. PO Resp. 24–25. But Patent Owner has withdrawn its MTA. Ex. 3003. As we stated, the MTA and related papers "have no further effect" upon the course of this proceeding. Paper 17, 2–3.

After reviewing the record, we find Petitioner's analysis persuasive and adopt it as our own. *See* Pet. 12–26. Thus, we determine Petitioner demonstrates by a preponderance of the evidence that Aerschot, because of its disclosures of compounds 12a and 15a, anticipates claim 1.

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[5] Aerschot identifies compound 15a as 1-(2-Fluoro-2,3-dideoxy-(β-D-*threo*-pentofuranosyl)-5-methylcytidine. Ex. 1004, 1747. Petitioner contends, and Patent Owner does not dispute, that "5-methylcytidine (as used in Aerschot) and 5-methylcytosine (as used in claim 1 in the list of possible nucleobases that could satisfy the B^n limitation) are merely two different names for the same nucleobase." Pet. 24 (citing Ex. 1003 ¶ 111).

F. Alleged Anticipation of Claim 2

Petitioner asserts that Aerschot anticipates claim 2. Pet. 26–30. After reviewing the entire record developed at trial, and as explained below, we determine that Petitioner has shown, by a preponderance of the evidence, that Aerschot anticipates claim 2.

Relevant to this case, claim 2, like claim 1, is directed to a compound of Formula Ia or Ib, and recites J is H, R^4 is the -halo fluorine, R^6 is—H, and "B^n is hydrogen or an optionally substituted nucleobase optionally functionalized at each exocyclic amine with an amine protecting group." Ex. 1001, 114:35–117:52. Claim 2 specifies that the claimed compound "is not represented by" certain recited structural formulas.

Petitioner contends that the genus of claim 2 encompasses the same thymine compound and the same 5-methylcytosine compound as discussed in claim 1. Pet. 29 (citing Ex. 1003 ¶¶ 126–131). According to Petitioner, neither compound is excluded from the scope of claim 2 by the proviso at the end of claim 2. *Id.* at 29 n.3 (citing Ex. 1003 ¶ 130). Petitioner asserts that, "[f]or the reasons discussed above for Claim 1, Aerschot discloses, enables, and anticipates each of those two species of Claim 2." *Id.* at 29 (citing Ex. 1003 ¶ 132).

Patent Owner does not dispute Petitioner's anticipation challenge of claim 2. *See* PO Resp. 25–26; Sur-reply 14. Instead, Patent Owner contends that the challenge to claim 2 is moot subject to the MTA. PO Resp. 25–26. But Patent Owner has withdrawn its MTA. Ex. 3003. As we stated, the MTA and related papers "have no further effect" upon the course of this proceeding. Paper 17, 2–3.

After reviewing the record, we find Petitioner's analysis persuasive and adopt it as our own. *See* Pet. 26–30. Thus, we determine Petitioner demonstrates by a preponderance of the evidence that Aerschot, because of its disclosures of compounds 12a and 15a, anticipates claim 2.

III. MOTION TO SEAL

Petitioner filed a Motion to Seal. Paper 19 ("Motion" or "Mot."). With the Motion, Petitioner filed a Protective Order that deviates from the Board's default protective order. Mot. 6; Exs. 1025 (clean copy), 1029 (showing marked-up comparison). According to Petitioner, Patent Owner does not oppose the entry of the proposed protective order. Mot. 6. The Protective Order (Ex. 1025) is hereby entered. It governs the conduct of the proceeding unless otherwise modified.

There is a strong public policy for making all information filed in an *inter partes* review open to the public, especially because the proceeding determines the patentability of claims in an issued patent and, therefore, affects the rights of the public. Generally, all papers filed in an *inter partes* review shall be made available to the public. *See* 35 U.S.C. § 316(a)(1); 37 C.F.R. § 42.14. Our rules, however, "aim to strike a balance between the public's interest in maintaining a complete and understandable file history and the parties' interest in protecting truly sensitive information." Patent Trial and Appeal Board Consolidated Trial Practice Guide 19 (November 2019) ("TPG").[6] Thus, a party may move to seal certain information (37 C.F.R. § 42.14); but only "confidential information" is protected from disclosure (35 U.S.C. § 326(a)(7)). Confidential information

[6] *Available at* https://www.uspto.gov/TrialPracticeGuideConsolidated.

means trade secret or other confidential research, development, or commercial information. 37 C.F.R. § 42.2.

The standard for granting a motion to seal is "for good cause." 37 C.F.R. § 42.54(a). The party moving to seal bears the burden of proof and must explain why the information sought to be sealed constitutes confidential information. *Id.* § 42.20(c).

Petitioner seeks to seal portions of the Sur-Reply as well as Exhibits 2048 and 2049.[7] Mot. 2. According to Petitioner, these files contain its confidential information. *Id.* at 2–4. Petitioner proposes redacting the files and summarizes the nature of the proposed redaction. *Id.* at 5–6. Patent Owner has since filed the redacted version of the Sur-Reply as well as Exhibits 2048 and 2049.

Upon review of Petitioner's Motion and the proposed redactions, we are persuaded that good cause exists to seal portions of the Sur-Reply as well as Exhibits 2048 and 2049.

Petitioner also filed its Opposition to Patent Owner's MTA (Paper 13), its Reply to Patent Owner's Response (Paper 14), and its Motion to Seal (Paper 19), as well as Exhibits 1005–1026 as "Board and Parties Only" with no corresponding motion to seal. If Petitioner wishes for any of these Papers and Exhibits to remain sealed, Petitioner should file a motion to seal and explain in detail what good cause supports granting the motion. In the absence of such a motion, at the expiration of ten business days from the

[7] Patent Owner originally also filed Exhibits 2046 and 2047 under seal. Petitioner states that those documents "can be made publicly available." Mot. 2. Patent Owner has since filed Exhibits 2046 and 2047 as public documents. Thus, we will expunge Exhibits 2046 and 2047 originally filed under seal.

date of this Decision, the entirety of Petitioner's Opposition to Patent Owner's MTA (Paper 13), Reply to Patent Owner's Response (Paper 14), and Motion to Seal (Paper 19), as well as Exhibits 1005–1026 will be made available to the public.

IV. CONCLUSION[8]

After reviewing the entire record and weighing evidence offered by both parties, we determine that Petitioner has met its burden to show, by a preponderance of the evidence, that Aerschot anticipates claims 1 and 2.

In summary:

Claims	35 U.S.C. §	References	Claims Shown Unpatentable	Claim(s) Not Shown Unpatentable
1	102	Aerschot	1	
2	102	Aerschot	2	
Overall Outcome			1, 2	

[8] Should Patent Owner wish to pursue amendment of the challenged claims in a reissue or reexamination proceeding subsequent to the issuance of this decision, we draw Patent Owner's attention to the April 2019 Notice Regarding Options for Amendments by Patent Owner Through Reissue or Reexamination During a Pending AIA Trial Proceeding. *See* 84 Fed. Reg. 16,654 (Apr. 22, 2019). If Patent Owner chooses to file a reissue application or a request for reexamination of the challenged patent, we remind Patent Owner of its continuing obligation to notify the Board of any such related matters in updated mandatory notices. *See* 37 C.F.R. §§ 42.8(a)(3), (b)(2).

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that Petitioner has shown, by a preponderance of the evidence, that claims 1 and 2 of the '569 patent are unpatentable;

FURTHER ORDERED that Petitioner's Motion to Seal is granted;

FURTHER ORDERED that Petitioner may, within five business days of this Decision, file an appropriate motion to seal as instructed in this Decision; and

FURTHER ORDERED that, because this is a Final Written Decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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