UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/605,669	10/16/2003	Wayne L. Ryan	1251-048	2668

25215 7590 08/21/2020

The Dobrusin Law Firm P.C.
29 W. Lawrence Street
Suite 210
Pontiac, MI 48342

EXAMINER	
MCNEIL, STEPHANIE A N	

ART UNIT	PAPER NUMBER
1653	

NOTIFICATION DATE	DELIVERY MODE
08/21/2020	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

dobrusin_PAIR@firsttofile.com
patmail@patentco.com
rmasquelier@patentco.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte WAYNE L. RYAN

Appeal 2020-000655
Application 10/605,669
Technology Center 1600

Before JEFFREY N. FREDMAN, TAWEN CHANG, and RACHEL H. TOWNSEND, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal[1,2] under 35 U.S.C. § 134 involving claims to a method for collecting mammalian blood cells. The Examiner rejected the claims as obvious and on the grounds of obviousness-type double patenting. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

---

[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the Real Party in Interest as Streck Inc. (*see* App. Br. 2).

[2] We have considered and refer to the Specification of Oct. 16, 2003 ("Spec."); Final Action of Aug. 15, 2018 ("Final Act."); Appeal Brief of May 15, 2019 ("Appeal Br."); and Examiner's Answer of Sept. 3, 2019 ("Ans.").

Statement of the Case

Background

"In biological and biochemical analysis, and related arts, it is often necessary to collect and preserve biological tissues (i.e., cells and cellular components), for useful periods of time" (Spec. ¶ 1). "The primary objective of tissue preservation is to provide as much structural detail of cells and components thereof as possible" (*id.* ¶ 4). "Thus, it is desirable in the art to obtain a method and a collection device that maintain the cells in their original unaltered morphology and preserve their antigenic sites" (*id.).* However, the "usual formulations for preservation of cells contain one or more agents, which react vigorously with the proteins of the cells to denature and insolubilize the components of the cell" (*id.* ¶ 5). "[I]t is also desirable to develop a method and a collection device that allow transportation (e.g., from the collection site to the analysis site) of the cells in ambient temperature" (*id.* ¶ 6).

The Claims

Claims 1, 4, 8, 10, 27, 31, 40, 45–47 and 52–61 are on appeal. Independent claim 1 is representative and reads as follows:

> 1. A method for collecting mammalian blood cells, comprising steps of:
>
> (a) providing a tube including preloaded compounds consisting of
>
> (i) ethylene diamine tetra acetic acid (EDTA) and
>
> (ii) diazolidinyl urea, the tube having an open end and a closed end that receives cells collected directly from a blood draw and wherein a majority of an interior portion of the tube is substantially free of contact with the preloaded components;
>
> (b) drawing a blood sample containing a plurality of blood cells into the tube whereby it contacts the preloaded compounds to yield a final composition, wherein a ratio of a volume of the preloaded compounds to a combined volume of the blood sample and the

preloaded compounds is from about 1:100 to about 2:100, and so that blood cells of the blood sample are stabilized directly and immediately upon blood draw; and

(c) transporting the blood sample, wherein the blood sample is drawn and transported in the same tube with no processing steps between blood draw and transporting.

The Issues

A. The Examiner rejected claims 1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, and 61 under 35 U.S.C. § 103(a) as obvious over Ryan,[3] Camiener,[4] Zelmanovic,[5] and Ames[6] (Ans. 3–8).

B. The Examiner rejected claims 8, 52, and 59 under 35 U.S.C. § 103(a) as obvious over Ryan, Camiener, Zelmanovic, Ames, and Deindoerfer[7] (Ans. 8–9).

C. The Examiner rejected claims 1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, and 61 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over: claims 1, 5, 6 of US 5,459,073; claims 9, 11, 12 of US 5,977,153; claims 1, 5 of US 7,419,832; claims 1–34 of US 6,337,189; claims 1–9 of US 7,767,460; each separately in view of Ryan, Camiener, Zelmanovic, and Ames (Ans. 9–17).

D. The Examiner rejected claims 8, 52, and 59 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, 6 of US 5,459,073; claims 9, 11, 12 of US 5,977,153; claims 1, 5 of US 7,419,832; claims 1–34 of US 6,337,189; claims 1–9 of US

---

[3] Ryan, W., US 5,849,517, issued Dec. 15, 1998.
[4] Camiener, G., US 5,977,153, issued Nov. 2, 1999.
[5] Zelmanovic et al., US 5,817,519, issued Oct. 6, 1998.
[6] Ames et al., *An Appraisal of the "Vacutainer" System for Blood Collection*, 12 Ann. Clin. Biochem 151 (1975).
[7] Deindoerfer et al., US 3,874,384, issued Apr. 1, 1975.

7,767,460; each separately in view of Ryan, Camiener, Zelmanovic, Ames, and Deindoerfer (Ans. 14–17).

E. The Examiner provisionally rejected claims 1, 8, 27, 40, 45–47, 52, 54, 55, 59, 60 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 54, 57, 64–66, 70, and 72 of copending US application 12/850,269 alone, or in combination with Ryan, Camiener, Zelmanovic, and Ames (Ans. 17–18).

A–D Obviousness and Obviousness-type double patenting

We will consider rejections A–D together because these four obviousness and obviousness-type double patenting rejections share the same issues and substantially the same prior art.

The issues with respect to these rejections are:

(i) Does a preponderance of the evidence of record support the Examiner's conclusion that the combination of prior art renders claim 1 obvious?

(ii) If so, has Appellant provided evidence of commercial success that, when considered with the prima facie case, results in a finding that the evidence considered as a whole does not support the obviousness of claim 1?

Findings of Fact

1. Ryan teaches:

> Patient samples are treated by mixing them directly with a preferred fixative solution of the present invention. The preferred ratio of sample to reagent is 1:1 but a ratio as low as 1:4 or as high as 2:1 is acceptable. For example, 1 ml peripheral blood is added to a vial containing 1 ml fixative solution, mixed and stored at 4° C.

(Ryan 8:35–40).

2. Ryan teaches a "preferred fixative solution of the present invention comprises imidazolidinyl urea (IDU), polyethylene glycol and EDTA, preferably in a buffered physiological salt solution" (Ryan 4:23–26).

3. Ryan teaches: "In a preferred embodiment of the present invention, the fixative solution comprises diazolidinyl urea (Du) and/or imidazolidinyl urea (IDU) in a buffered physiological salt solution. In a highly preferred embodiment, the fixative solution further comprises polyethylene glycol and EDTA" (Ryan 7:9–14).

4. Ryan teaches the "preferred concentration of Du is from about 1 % to about 20% by weight" (Ryan 4:49–50).

5. The Examiner finds that in Ryan's

> preferred final composition containing both sample and fixative, DU is present at about 0.5% to about 10% (that is, the 1–20% DU solution is diluted 1:1 with the sample). "0.5%" is mathematically equivalent to "0.5:100" and "1:200." Regarding claims 31 and 53, Ryan teaches fixative solutions containing 50g DU in 1 liter total, i.e. 0.05 g of DU per ml of fixative solution.

(Final Act. 3).

6. Ryan teaches the "use of Du preserves the cell structure, nucleic acids, and cell antigens. Thus, the sample can be transported or held in the lab for several days" (Ryan 9:13–15).

7. Camiener teaches a "solution was prepared using citric, alkane-sulfonic, glycolic, and salicylic acids plus diazolidinyl urea at a molar ratio of 1.8. The material was evaporated . . . The reactive group content and fixative activity was found to be unchanged" (Camiener 9:9–15).

8. Camiener teaches blood may be preserved using the disclosed compositions (*see* Caminer 7:42–47) and ingredients may include "chelating agents (such as EDTA and its alkali metal or ammonium salts), all of which are used in a conventional manner in fixative solutions" (Camiener 8:13–15).

9. Zelmanovic teaches "solutions of sodium citrate or K_3EDTA can be mixed with a blood sample . . . about 7 to 14 mg of K_3EDTA in powder form are used per 7 cc tube" (Zelmanovic 18:27).

10. Ames teaches vacutainer tubes that may contain EDTA (*see* Ames 151).

Principles of Law

A prima facie case for obviousness "requires a suggestion of all limitations in a claim," *CFMT, Inc. v. Yieldup Int'l Corp*., 349 F.3d 1333, 1342 (Fed. Cir. 2003) and "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc*., 550 U.S. 398, 418 (2007).

Analysis

Claim Interpretation

We begin with claim interpretation, since before a claim is properly interpreted, its scope cannot be compared to the prior art or analyzed for patent eligibility. We find two limitations that require interpretation. First, independent claims 1, 27, and 40 each recite a step requiring a collection

container/tube that is "preloaded" with or "contains preloaded" "compounds consisting of: (i) ethylene diamine tetra acetic acid (EDTA); and (ii) diazolidinyl urea." Second, these claims also have a volumetric ratio requirement: that "a ratio of a volume of the preloaded compounds to a combined volume of the blood sample and the preloaded compounds is from about 1:100 to about 2:100" (claim 1); "ratio of a volume of the preloaded compounds to a volume of the final composition is from about 1:100 to about 2:100" (claims 27 and 40).

> *"collection container preloaded compounds consisting of: (i) ethylene diamine tetra acetic acid (EDTA); and (ii) diazolidinyl urea"*

It is well settled that the transitional phrase "consisting of" excludes any element, step, or ingredient not specified in the claim. *In re Gray*, 53 F.2d 520 (CCPA 1931). Thus, the use of the transitional phrase "consisting of" suggests that the collection container contains solely EDTA and diazolidinyl urea. This understanding is consistent with Appellant's amendment filed May 2, 2016, where Appellant contends "the preloaded contents have been limited to IDU, EDTA, and glycine" and cites MPEP 2111.03 regarding the limiting effect of "consisting of" (*see* Amdt. 5/2/2016 at 5). The claims were further limited to only EDTA and diazolidinyl urea in the Amendment filed April 12, 2018 (*see* Amdt 4/12/2018 at 2).

We therefore interpret the claim to require a collection container containing compounds that are solely EDTA and diazolidinyl urea.

> *"ratio of a volume of the preloaded compounds to a combined volume of the blood sample and the preloaded compounds is from about 1:100 to about 2:100"*

The Specification's explains that the "preloading step 204 may optionally include freeze drying the compounds in the tube 12" (Spec. ¶ 29).

Thus, the Specification encompasses both liquid and dry formulations. However, in the amendment filed January 3, 2012, Appellant deleted the limitation "drying the compounds" (*see* Amdt 1/3/2012 at 2), suggesting that the claim recites compounds in the tube in liquid form. The claim itself, by using the phrase "volume of the preloaded compounds" also reasonably supports a finding that the preloaded compounds are in liquid form.

Therefore, we interpret the claim to require a liquid volume of the preloaded compounds that is between 1:100 to about 2:100 relative to the liquid volume of the blood sample added in combination with the preloaded compounds.

Obviousness

Appellant contends "Ryan does not teach preloading DU and EDTA into the sample collection tube" and contends that even if "Camiener suggests a composition comprising EDTA and DU
. . . . the Final Office Action has not established that Camiener teaches compounds **consisting of EDTA and DU**" (Appeal Br. 22). Appellant also contends "above, Ryan appears to teach away from a volume ratio of 'about 1:100 to about 2:100', as that is clearly not within the acceptable volume range disclosed above in Ryan" (Appeal Br. 20; *cf*. FF 1).

The Examiner responds that "it is the primary reference Ryan who teaches collecting the blood sample into an EDTA vacutainer, and that it is useful to also combine a DU fixative with this blood EDTA mixture" (Ans. 19). The Examiner responds to the ratio issue by finding that

> Ryan teaches contacting 1 ml of the biological sample with 1 ml of DU solution, and that Ryan therefore teaches that in the preferred final composition containing both sample and DU fixative, the DU is present at about 0.5% to about 10% (that is, the 1–20% DU solution is diluted 1: 1 with the sample). As explained above, "0.5%" is

> mathematically equivalent to "0.5:100" and "1:200." Moreover, it is noted that even Ryan's teaching of amounts as low as 1%, before the dilution, also read on the claimed amount. Furthermore, the rejection above states that it is obvious to use preloaded dried DU with the EDTA in Ryan's method, not only a diluted DU as applicant alleges.

(Ans. 18–19).

We agree with Appellant on both issues. As to the recitation of "consisting of," the Examiner does not identify a teaching in Ryan, Camiener, Zelmanovic, Ames, or Deindoerfer that teaches a solution composed solely of EDTA and diazolidinyl urea. Ryan does teach a fixative composed of "imidazolidinyl urea (IDU), polyethylene glycol and EDTA, preferably in a buffered physiological salt solution" (FF 2; *cf*. FF 3), but this fixative does not consist of the urea and EDTA compounds alone, but also includes polyethylene glycol and a salt solution. The Examiner provides no persuasive reasoning explaining why a fixative composition solely composed of EDTA and diazolidinyl urea as required by all of the independent claims would be obvious.

As to the limitation reciting a "a volume of the preloaded compounds to a combined volume of the blood sample and the preloaded compounds is from about 1:100 to about 2:100," the Examiner interprets this as encompassing the situation where equal volumes of fixative and blood may be used, so long as the amount of diazolidinyl urea in the fixative solution is only 1% of the total volume. Consistent with our claim interpretation above, we understand the claims to require that the total volume of the preloaded fixative solution itself is between 1% and 2% of the blood sample plus preloaded fixative. Therefore, when a volume of blood sample is being added to the tube such that the combined volume of the blood and preloaded fixative is 1 ml, the volume of the preloaded fixative solution must be

between about 10 µl and 20 µl, not a 1 ml fixative solution that only has between about 10 µl and 20 µl of diazolidinyl urea and EDTA along with solvents.

While we do not agree with Appellant that Ryan teaches away, because Ryan does not discredit the use of volumes outside the preferred ratios (FF 1), and we recognize that the volume of fixative solution is an optimizable variable as argued by the Examiner (*see* Ans. 21), we find "[m]issing from the . . . analysis is an explanation as to why it would have been routine optimization to arrive at the claimed invention." *In re Stepan Co.*, 868 F.3d 1342, 1346 (Fed. Cir. 2017). In this case, the Examiner provides no explanation as to why the ordinary artisan would have had either reason to modify Ryan's ratio of 1:4 and optimize to a 1:100 or 2:100 ratio as recited by the claims or a reasonable expectation of success in doing so.

We therefore conclude that the Examiner has not established a prima facie case of obviousness.

Commercial success

We recognize the commercial success data submitted by Appellant in the Owen Declarations dated Dec. 21, 2011 and Jan. 9, 2015. We do not find the evidence particularly persuasive because the evidence only shows an increase in sales of Cyto-Chex BCT product relative to the Streck Cell Preservative product, but does not demonstrate growth relative to other manufacturers. That is, the market is limited to "direct draw tubes for long term stabilization" but evidence simply shows that the market itself grew, not that there was any preference for the product at issue.

In any case, we need not rely upon the commercial success information because the Examiner did not establish a prima facie case of obviousness.

Conclusion of Law

(i) A preponderance of the evidence of record does not support the Examiner's conclusion that the combination of references renders the claims obvious.

(ii) Appellant has provided some evidence of commercial success but we need not rely upon this evidence in view of the unpersuasive prima facie case of obviousness.

E. Provisional Double Patenting

When application on appeal is provisionally rejected based on later-filed application, and all other rejections on appeal are reversed, the proper course is not to reach the provisional obviousness-type double patenting rejection. *Ex parte Moncla*, 95 USPQ2d 1884 (BPAI 2010). Here, US application 12/850,269 remains pending and an Appeal Brief was filed on May 20, 2020. Thus, we do not reach the provisional double patenting rejection over claims 54, 57, 64–66, 70, and 72 of that application. (According to MPEP § 804, if the double-patenting rejection is the only one remaining in the senior application, the Examiner should withdraw the ODP rejection and require a TD in the junior application.)

CONCLUSION

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, 61	103	Ryan, Camiener, Zelmanovic, Ames,		1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, 61
8, 52, 59	103	Ryan, Camiener, Zelmanovic,		8, 52, 59

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
		Ames, Deindoerfer		
1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, 61	Obviousness-type Double Patenting	US 5,459,073, Ryan, Camiener, Zelmanovic, Ames		1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, 61
1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, 61	Obviousness-type Double Patenting	US 5,977,153, Ryan, Camiener, Zelmanovic, Ames		1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, 61
1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, 61	Obviousness-type Double Patenting	US 7,419,832, Ryan, Camiener, Zelmanovic, Ames		1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, 61
1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, 61	Obviousness-type Double Patenting	US 6,337,189, Ryan, Camiener, Zelmanovic, Ames		1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, 61
1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, 61	Obviousness-type Double Patenting	US 7,767,460, Ryan, Camiener, Zelmanovic, Ames		1, 4, 10, 27, 31, 40, 45–47, 53–58, 60, 61
8, 52, 59	Obviousness-type Double Patenting	US 5,459,073, Ryan, Camiener, Zelmanovic, Ames, Deindoerfer		8, 52, 59
8, 52, 59	Obviousness-type Double Patenting	US 5,977,153, Ryan, Camiener, Zelmanovic, Ames, Deindoerfer		8, 52, 59
8, 52, 59	Obviousness-type	US 7,419,832, Ryan, Camiener,		8, 52, 59

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
	Double Patenting	Zelmanovic, Ames, Deindoerfer		
8, 52, 59	Obviousness-type Double Patenting	US 6,337,189, Ryan, Camiener, Zelmanovic, Ames, Deindoerfer		8, 52, 59
8, 52, 59	Obviousness-type Double Patenting	US 7,767,460, Ryan, Camiener, Zelmanovic, Ames, Deindoerfer		8, 52, 59
1, 8, 27, 40, 45–47, 52, 54, 55, 59, 60	Provisional Obviousness-type Double Patenting	US application 12/850,269		
Overall Outcome				1, 4, 8, 10, 27, 31, 40, 45–47, 52–61

REVERSED