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.
13/091,209	04/21/2011	Daniela Cocconi	378507US68	4141

22850 7590 01/30/2019

OBLON, MCCLELLAND, MAIER & NEUSTADT, L.L.P.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER
BABSON, NICOLE PLOURDE

ART UNIT	PAPER NUMBER
1619	

NOTIFICATION DATE	DELIVERY MODE
01/30/2019	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):

patentdocket@oblon.com
OBLONPAT@OBLON.COM
iahmadi@oblon.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte DANIELA COCCONI and ROSSELLA MUSA

Appeal 2017-005475
Application 13/091,209[1]
Technology Center 1600

Before DEBORAH KATZ, RACHEL H. TOWNSEND, and DAVID COTTA, *Administrative Patent Judges*.

COTTA, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims directed to a process for preparing a dry powder formulation for inhalation. The Examiner rejected the claims on appeal under 35 U.S.C. § 103(a) as obvious.

We affirm.

---

[1] According to Appellants, the real party in interest is Chiesi Framaceutici S.p.A. App. Br. 2.

STATEMENT OF THE CASE

The Specification discloses that "[d]ry powder inhalation (DPI) drug therapy has been used for many years to treat respiratory conditions such as asthma, chronic obstructive pulmonary disease (COPD), and allergic rhinitis." Spec 1. "During the various manufacturing operations (milling, mixing, transport and filling), powders accumulate electrostatic charges from inter-particulate collisions and contact with solid surfaces (*e.g.* vessel walls)." *Id.* at 2. According to the Specification, "the reduction of electrostatic chargeability may improve the flow properties during the operations of the manufacture process (sieving, pouring) and during the filling of the inhaler" which could lead to "improved homogeneity of the active ingredient in the formulation, and hence to an improved reproducibility and accuracy of the delivered dose and the fine particle dose." *Id.* at 3. It would thus be "highly advantageous to provide a process for preparing powder formulations . . . capable of reducing electrostatic charges, and hence improving their performance characteristics." *Id.* The Specification discloses "processes for preparing dry powder formulations for inhalation . . . having reduced electrostatic charges." *Id.* at 1.

Claims 1, 11, and 12 are on appeal. Claim 1 is illustrative and reads as follows:

> 1. A process for preparing a dry powder formulation for inhalation, comprising one or more active ingredients selected from the group consisting of a β2-adrenoceptor agonist and a corticosteroid, and carrier particles, said carrier particles comprising:
>
> (i) a fraction of co-micronized particles made of a mixture of alpha-lactose monohydrate and magnesium stearate,

> the mixture having a mass median diameter (MMD) lower than 20 microns; and
>
> (ii) a fraction of alpha-lactose monohydrate coarse particles having a mass diameter of 212 to 355 microns,
>
> said process comprising:
>
> (a) co-micronizing said alpha-lactose monohydrate and said magnesium stearate particles, to obtain co-micronized particles;
>
> (b) mixing said co-micronized particles with said coarse alpha-lactose monohydrate particles for at least four hours to spheronize them, to obtain said carrier particles; and
>
> (c) mixing said carriers particles with said one or more active ingredients,
>
> wherein said co-micronized particles are first conditioned by exposure to a relative humidity of 50 to 70% at a temperature of 22 ± 2 °C for a time of 48 hours, prior to said mixing.

App. Br. 13.

The Examiner rejected claims 1, 11, and 12 under 35 U.S.C. § 103(a) as obvious over the combination of Staniforth,[2] Briggner,[3] and Morton.[4]

[2] Staniforth et al., US Patent Publication No. 2003/0180227 A1, published Sep. 25, 2003 ("Staniforth").
[3] Briggner et al., US Patent No. 5,874,063, issued Feb. 23, 1999 ("Briggner").
[4] Morton et al., US Patent Publication No. 2008/0063719 A1, published Mar. 13, 2008 ("Morton").

ANALYSIS

Appellants argue claims 1, 11, and 12 together. We designate claim 1 as representative.

Staniforth discloses a "dry powder for inhalation . . . into the low respiratory tract of patients . . . which can be produced in a simple way." Staniforth Abstract. In finding claim 1 obvious, the Examiner found that Staniforth disclosed most of the elements of claim 1. Final Act. 3–4.[5] The Examiner acknowledged, however, that Staniforth did not disclose a step in which "co-micronized particles are first conditioned by exposure to a relative humidity of 50 to 75% at a temperature of 22 ±2 °C for a time of 48 hours, prior to said mixing." *Id.* at 4. The Examiner relied on Briggner and Morton to remedy this deficiency. *Id.*

The Examiner found that Briggner disclosed a "treatment method of increasing the stability of a pharmaceutical fine particle mixture" useful for inhalation including "exposure to 35–85% humidity at ambient temperature (i.e. about 22 ºC) for a variable length of time." *Id.* The Examiner noted that Briggner's humidity overlapped with the claimed range and that Briggner exemplified exposure only for 24 hours. *Id.* The Examiner found that Morton also disclosed a treatment method for inhalable pharmaceutical compositions comprising a dry powder. *Id.* According to the Examiner, Morton teaches "exposure to 30–100%, 40–95%, 50–90% and exemplify[ies] 60% relative humidity at 10–50 °C or 25 °C for 48 hrs" in order to "remove amorphous material" from the fine particle mixture. *Id.* at 5.

[5] Office Action mailed April 20, 2016 ("Final Act.").

Based on the combined disclosures of Staniforth, Briggner, and Morton, the Examiner concluded that it would have been obvious to "include a conditioning step at a relative humidity of 50 to 75% at a temperature of 22 ±2 °C for a time of 48 hours in the process of Staniforth." *Id.* at 5. The Examiner explained that Staniforth, Briggner, and Morton were all drawn to fine particle mixtures for inhalation and that the skilled artisan would have been motivated to include a conditioning step "in order to increase the formulation stability and to increase the respirable fraction of the active powder, as taught by Briggner." *Id.* The Examiner noted that Briggner teaches varying the time necessary for the conditioning step based on a number of factors and that the skilled artisan would have included the conditioning step prior to the spheronization step because Briggner teaches that the conditioning step is inappropriate after the fine particles have been spheronized. *Id.*

We adopt the Examiner's findings of fact and reasoning regarding the scope and content of the prior art (Ans. 3–8; Final Act. 2–9) and agree that the claims are obvious over Staniforth, Briggner, and Morton. We address Appellants' arguments below.

Appellants contend that all of the excipients disclosed in Briggner's fine powders are either hydrophilic or hygroscopic. App. Br. 8 (citing Cocconi Decl.[6] ¶ 16). Appellants further contend that "co-micronizing alpha-lactose monohydrate and magnesium stearate particles [as disclosed in Staniforth] renders the co-micronized particles moisture resistant and ***hydrophobic.***" *Id.* According to Appellants' inventor, Dr. Cocconi, "[s]ince

[6] Declaration of Dr. Daniela Cocconi under 37 C.F.R. § 1.132, filed January 29, 2016 ("Cocconi Decl.").

the co-micronized particles used in the process of the above-identified application are already hydrophobic and moisture resistant, one of skill in the art would have had no motivation to apply the treatment of Briggner et al. to these co-micronized particles." Cocconi Decl. ¶ 20. We are not persuaded.

Staniforth teaches that "co-micronising the excipient particles and the magnesium stearate particles . . . partially coat[s] the surface of the excipient particles." Staniforth ¶ 59. As the Examiner points out, this "would leave some area uncoated by the magnesium stearate and available for particle aggregation," which would have provided a reason to treat the particles with humidity. Ans. 6. Appellants argue that the Examiner's conclusion that the partially coated particles would tend to aggregate is "not supported by facts adequate to outweigh the evidence provided in [the Cocconi] Declaration." Reply Br. 5. But the Cocconi Declaration does not specifically address the effect of a partial magnesium stearate coating, and Staniforth clearly teaches that its particles may be only partially coated.

In addition, Morton teaches the use of force control agents to "reduce the cohesion between the fine particles within [a] powder formulation, thereby promoting deagglomeration upon dispensing the powder from the dry powder inhaler." Morton ¶ 48. Among the suitable force control agents disclosed is magnesium stearate. *Id.* ¶ 51. Importantly, Morton teaches that "formation of hard agglomerates occurs within a micronised powder that contains surface non-crystalline material, *whether formulated with excipient, any moisture protection agent, a force control agent, or on its own*." *Id.* ¶ 30 (emphasis added); *see also, id.* ¶ 119 ("it was concluded that magnesium stearate was not providing protection from instability in . . .

prototype formulations"). This suggests agglomeration occurs in a micronized powder – like that disclosed in Staniforth – even when that powder has been treated with magnesium stearate. Consistent with this disclosure, Morton discloses that for "best results," "a force control agent" – like magnesium stearate – is used in combination with other methods of preventing agglomeration like "suitable conditioning," which Morton teaches may include exposure to humidity. *Id.* ¶¶ 51, 57, 160. Morton thus provides additional reason to apply the claimed humidity treatment to Staniforth's co-micronized particles

Appellants would have us discount Morton's teachings on the basis that Morton is "directed to the treatment of an active ingredient (an antimuscarinic agent) for increasing its stability over time and not to a treatment of a mixture of excipients for improving the flow properties." Cocconi Decl. ¶ 23; *see also,* Reply Br. 5 (citing same). We are not persuaded because many of the dry powder compositions disclosed in Morton include excipients, and neither Appellants nor Dr. Cocconi provide persuasive evidence suggesting that considerations for preventing agglomeration of compositions comprising an antimuscarinic agent would not also apply to preventing agglomeration of a mixture of excipients.

Accordingly, we affirm the Examiner's rejection of claim 1 as obvious. Because they were not argued separately, claims 11 and 12 fall with claim 1.

SUMMARY

For the reasons discussed herein, and those set forth in the Examiner's Answer and Final Office Action, we affirm the Examiner's rejection of

claims 1, 11, and 12 under 35 U.S.C. § 103(a) as obvious over the combination of Staniforth, Briggner, and Morton.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a). *See* 37 C.F.R. § 1.136(a).

AFFIRMED