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2023, May 4
OUR REF : PNAT45301-RUP DELHI
YOUR REF : 201917004058
ATTENTION : SARAVANA RAM PRASAD V G
(CONTROLLER OF PATENTS & DESIGNS)

RESPONSE TO THE FIRST EXAMINATION REPORT
LAST DATE : 24 MAY 2023

Dear Sir/Madam,

Re : INDIA
SANOFI
INDIAN PATENT APPLICATION NO. 201917004058
FILED ON 01 February 2019
Title : ANTIBODY FORMULATIONS
Corresponding PCT Application No. : PCT/EP2017/066803 Dated 05 July 2017
Priority Details: 62/358,404 Dated 05 July 2016 of UNITED STATES OF AMERICA
16306090.8 Dated 30 August 2016 of EUROPE

In response to First Examination Report (FER) dated 24th November 2022, in respect of the above-identified patent application, we are submitting the under-noted documents with amended claim pages 58-60, fresh abstract, fresh drawings (13 sheets). The previously pending claim pages, original abstract, and original drawings, which were not returned with the FER, may please be treated as cancelled. In this connection, we respectfully submit as

under, for and on behalf of our client, the applicant herein:

(B)(1) - (B)(4) & (B)(6) - (B)(10) In response to the objections raised by the Examiner, the applicant submits as under :

The statement of claims has been amended.

We are submitting **a marked up copy of claims and amended claim pages,** which may please be taken on record.

Claims 1-4, 6, 7, 14, and 21 have been canceled, and claims 5, 8-13, 15-20, and 22 have been amended. As renumbered, claims 1-14 are now pending. Support for the amendments to the claims can be found in the previously pending claims and, for example, in paragraphs [0003], [0093], and [0094] of the published PCT application.

Novelty, Inventive Step, & Non-Patentability

Claims 1-6, 8-13, and 15-22 are deemed to lack novelty over International Publication No. WO 2013/148686 A2, International Publication No. WO 2009/032661 A1, U.S. Patent Application Publication No. US 2014/0004106 A1, Wang et al. ("Antibody Structure, Instability, and Formulation," Journal of Pharmaceutical Sciences, 96(1):1-26, 2007), and Daugherty et al. ("Formulation and Delivery Issues for Monoclonal Antibody Therapeutics," Current Trends in Monoclonal Antibody Development and Manufacturing, 103-129, 2010).

In response, the claims have been amended to overcome the objection.

The FER also objects to claims 1-6, 8-13, and 15-22 as lacking inventive step over the

cited references. Applicant respectfully disagrees. In response, the applicant submits that the presently claimed antibody formulations successfully overcame a previously unrecognized problem in the art: the formation of "Stardust" particles, which occurred in antibody formulations, as described in Example No. 1 of the present application. The formation of "Stardust" particles had not been a recognized problem in the art.

As defined in paragraph [0096] of the specification, "'**Stardust**' particles are particles occurring in glass containers in association with the presence of an antibody formulation within the container." As discussed in Example 1, Stardust particles were observed in an antibody formulation prepared for a phase I clinical study. The formulation contained 100 mg/mL SAR 113244 monoclonal antibody, which is the same anti-CXCR5 antibody recited in the claims, arginine at 10 mg/mL, NaCl at 2 mg/mL, polysorbate 20 at 0.01 %, and citrate buffer at 10 mM and had a pH of 6. This formulation was stable in terms of chemical stability and sub-visible particles, **but after about one year of storage in glass containers, formation of "Stardust" particles occurred.** The formation of the particles caused the study to be stopped. No "Stardust" particles were observed when the formulation was stored in plastic containers. Therefore, it was suspected that "Stardust" particles may have occurred as a result of the formulation delaminating glass. A test was performed to investigate the possibility of glass delamination. As shown in Tables 4A and 4B, no glass delamination was observed even under accelerated conditions (12 weeks at 60°C). However, as shown in Table 5, glass component leaching was observed and believed to underlie, in part, the formation of "Stardust" particles. Further, it was believed that protein aggregation also contributed to the formation of "Stardust" particles. **Therefore, a new formulation was designed to avoid the leading to the currently claimed formulations.**

Example 2 describes the development and testing of the currently claimed formulation. As demonstrated in Table 9, Formulation B had unexpected resilience

against particle formation at high antibody concentrations under accelerated conditions (24 weeks at 40°C; see paragraph [00183]).

Further, the cited references are inapposite to the current invention.

D1 (WO 2013/148686) describes the formulations of CXCR5 antibodies that gave rise to the formation of "Stardust" particles. Therefore, the present application is a direct improvement over these formulations.

D2 (WO 2009/032661) describes the CXCR5 antibodies that were included in the formulations of D1, which gave rise to the formation of "Stardust" particles. Therefore, the present application is also a direct improvement over formulations that contained the antibodies disclosed herein.

D3 (US 2014/004106 A1) is equivalent to D1 and therefore cumulative over D1 (they each have the same disclosure). Therefore, the present application is a direct improvement over these formulations.

D4 (Wang et al.) and D5 (Daugherty et al.) are both considered "A" references, which are defined as documents "defining the general state of the art which [are] not considered to be of particular relevance." International Search Report, page 1. Therefore, these references are not relevant to the patentability of the pending claims.

In light of the fact that D1-D3 did not recognize that the antibodies and formulations disclosed therein would eventually give rise to the formation of "Stardust" particles, it follows logically that a skilled artisan could not have pursued potential solutions to an unrecognized problem based on the cited references. Nor could

there be a reasonable expectation of success for solving an unrecognized problem. For at least these reasons, Applicant submits that the pending claims are inventive over the cited references.

Thus, the claimed subject matter is both novel and inventive over the cited prior art documents.

As regards Section 3(d) and section 3(e) objections, as the claimed subject matter is novel and inventive, it ought not to be deemed to be a mere new form of a known substance or a mere aggregation of known substances to attract Section 3(d) or section 3(e) of the Act. The unexpected superior technical effect in terms of successfully overcoming a previously unrecognized problem in the art: the formation of "**Stardust**" particles. Hence, these objections may please be reviewed and withdrawn.

Claim 21 has been deleted, thereby rendering the objection under Section 3(i) moot.

Unity of Invention

In view of the deletion of claims 1-4, 6, 7, 14 and amendment of the remaining claims, the objection against alleged lack of unity have been rendered moot. All claims are now bound by a single inventive concept. The claims 1-4, 6, 7, 14 have been deleted without prejudice or disclaimer, and the applicant reserves the right to file one or more divisional application(s) with patentably distinct subject matter.

Sufficiency of Disclosure, Scope, Clarity and Conciseness, Definitiveness, & Other Requirements

The statement of claims have been substantially amended to recite the essential and

distinguishing features. The claimed antibody formulation has been specifically defined in terms of its ingredients and their weight % or proportion, which finds explicit support and basis in the specification.

The dependent claims now recite "as claimed in".

As regards the objected term "about", the applicant respectfully submits that "about" is given a specific definition in the specification in paragraph [0050], where it states, in relevant part, that "term 'about' . . . means within 10%, such as within 5% (or 1 % or less) of a given value or range." Therefore, Applicant respectfully submits that the term has a specified and a precise definition.

In view of the claim amendments, as currently carried out, and the arguments, as discussed above, these objections may please be reviewed and withdrawn.

Formal Requirements

Fresh abstract and fresh drawings are being submitted herewith, which may please be taken on record.

The statement of claims now start with the term "We Claim".

We are submitting an **updated Form 3, as available from Espacenet,** with copy of **US patent,** to meet the statutory requirement under Section 8**,** which may please be taken on record.

The applicant hopefully believes that in view of the above submissions and

amendments carried out in the claims, as discussed above, the Controller will find this application in a good condition for allowance.

It is respectfully requested that further objections and/or requirements, if any, in respect of the above identified patent application may please be sent to us at the earliest.

For and on behalf of the applicant herein, we would humbly pray to the Learned Controller of Patents & Designs that the applicant herein be given opportunity of being heard, before issuing any adverse decision, under Section 14 or 15 of the Act, following the Principles of Natural Justice.

Very truly yours,

(RUPSA GUPTA)
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Encl.: (**UPLOADED**)

1. Amended claim pages 58-60
2. Fresh Abstract
3. Fresh Drawings (13 sheets)
4. Marked-up copy of claims
5. Updated Form 3, as available from Espacenet
6. Section 8(2) document as mentioned above