Intellectual Property Appellate Board
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OA/03/2017/PT/CHN
FRIDAY, THIS THE 7TH DAY OF AUGIST, 2020

HON'BLE SHRI JUSTICE MANMOHAN SINGH **CHAIRMAN**
HON'BLE DR. ONKAR NATH SINGH **TECHNICAL MEMBER (PVPAT)**

1. **STEMPEUTICS RESEARCH PVT. LTD.**
AKSHAY TECH PARK #72 & 73 2nd FLOOR,
EPIP ZONE, PHASE – 1 AREA WHITEFIELD,
BANGALORE – 560 066, KARNATAKA, INDIA

…APPLICANT/APPELLANT
(Represented by:Mr.SaurabhAnand)

Versus

1. **THE ASSISTANT CONTROLLER OF PATENT & DESIGNS**
THE PATENT OFFICE,
INTELLECTUAL PROPERTY BUILDING, G.S.T.
ROAD, GUINDY, CHENNAI - 600 032

…RESPONDENT

(Represented by – None)

ORDER

HON'BLE SHRI JUSTICE MANMOHAN SINGH, CHAIRMAN

1. The present Appeal has been filed against the Order u/s 15 (hereinafter referred to as the "Order") of the Patents Act, 1970 (hereinafter referred to as "Act") passed by the Respondent, dated January 09, 2017 whereby the Respondent refused to grant the patent in respect of Indian patent application bearing No. 2932/CHE/2009 (hereinafter referred to as the "Present Application").

2. The relevant dates and events are as under:-

Date	Particulars
27.11.2009	Indian Patent Application filed at the Indian Patent Office with 16 Claims.

04.05.2012	Date of Publication
26.11.2010	Request for Examination filed
28.11.2013	First Examination Report (FER) was issued. The FER contained objections *inter-alia* on the ground that the complete specification is beyond the scope of its provisional specification, and that the claims 1-15 fall within the scope of Section 3(j) of the Act. The FER also raised objection on non-compliance of requirement u/s 7(2) of the Act as one of the inventors had not signed Form-I. The FER also stated that the question of novelty and inventive step will be considered after the above objections have been complied with.
06.02.2014	Reply to FER was filed along with arguments to overcome the objection raised in the FER.
10.09.2014	Hearing Notice issues with hearing fixed on 13.10.2014. Apart from maintaining objections on Section 3(j) and 7(2) of the Act, fresh objections raised under: - Section 2(1)(j) of the Act for lack of novelty and inventive step of claims 1-16 in view of three cited documents; - Section 3(e) of the Act for claims 11-16; - Lack of clarity and lack of support for claims in the description; - Section 6 of the Biodiversity Act, 2002; and - Form 1 and Section 10(4) of the Act.
13.10.2014	Hearing was conducted.
18.12.2014	Appellant filed its response to the hearing notice along with amended set of claims (claims 1-13) and annexures.
26.09.2016	Supplemental amendments to the claims (claims 1-12) along with amended specification filed.
09.01.2017	Decision of Refusal
10.04.2017	Appeal filed before this Board.

INVENTION CLAIM

3. The application relates to the field of "**Stem Cells**". Stem cells are the body's fundamental cells (raw materials) from which all other cells of the body with specialized functions are generated(e.g. blood cells, skin cells, fat cells, specialized cells of different organs and the like). It is related to "**Mesenchymal Stem Cells**" (hereinafter referred to as the "**MSC**" or "**MSCs**"). Mesenchymal Stem Cell is a specific type of StemCell which has the capacity to grow into specialized cells of the body such as bone cells,cartilage cells,blood cells, fat cells, muscle cellsetc.

The Artin the field of MSCs till the date of filing the present Application discloses products (compositions) containing MSCs of a single donor or individual donor (hereinafter referred to as the "single donor MSCs" or "individual donor MSCs" or "un-pooled MSCs") and corresponding methods of preparing such compositions containing said single donor MSCs. The Art as existing on the date of filing the present Application was teaching away from combining/pooling MSCs from different donors because when the stem cells from one individual was being injected to another individual, chances of rejection and associated complications are extremely high, due to complex compatibility issues that arise between the recipient and the donor.

4. The case of the appellant is that thePresent Applicationprovides compositions/productscomprising "Pooled MSCs" (*i.e.*combination of MSCs of Multiple Donors).Particularly, the present application provides a composition (final product) [Claim 11]comprising *pooled* MSCs along with ingredientshuman serum albumin (HSA), dimethyl sulfoxide (DMSO) and multiple electrolytes injections, type 1, USP; and a composition (termed as 'working cell bank') of Claim 12comprising *pooled* MSCs, fetal bovine serum (FBS) and dimethyl sulfoxide (DMSO). The said defined compositions of the present applicationare prepared by the following methods:

a) obtaining MSCs from a single donor and culturing them (i.e. growing) according to steps a) to h) of Claim 1 to prepare a

Master Cell Bank composition. This Master Cell Bank composition comprises MSCs of a single donor and multiple Master Cell Bank compositionsare prepared wherein each Master Cell Bank composition contains single donor MSCs;

b) pooling the MSCs (i.e. combining MSCs) from the 'multiple' Master Cell Bank compositions to obtain pooled MSCs followed by culturing the pooled MSCs according to steps c) to e) of Claim 3 to obtain the Working Cell Bankcomposition (Claim 12) comprising *pooled* MSCs, FBS and DMSO; and

c) additional culturing of the *pooled* MSCs of the Working Cell Bank composition according to steps b) to g) of Claim 6 to obtain the compositionor final product (Claim 11) comprising *pooled* MSCs, HSA, DMSO and multiple electrolytes injections, type 1, USP.

The Claims 11 and 12 relates to the compositions of "pooled MSCs"and the methods of preparing the compositions (Claims 1 to 10) lead to said compositions comprising "pooled MSCs".Said compositions comprising "Pooled" MSCs and methods leading to "Pooled" MSC productsisthe critical feature distinguishing the present application from Prior Art.

5. It is alleged that the compositions as claimed in the Present Application, more particularly Claims 11 and 12, has been successfully translated to practical treatment of medical conditions. It is s well-known in the art that medical applications of a cell-based product/drug must satisfy the important requirement of safety in addition to therapeutic efficacy (functional activity). Said requirement becomes more critical if the cell-based product or drug contains external donor cells. The compatibility issues arise when cells from an external donor is injected to a recipient (patient). For example, it is well known that when stem cells from one individual is injected to another individual, chances of rejection and

associated complications are extremely high, due to complex compatibility issues that arise between the recipient and the donor. This is particularly because the recipient's immune system treats the cells of donor as a foreign particle. Thus, it is stated that the immune system of the recipient attacks the donor cells as it would attack any foreign cell (e.g. bacteria or virus particles). The same leads to adverse immune reaction and rejection of the donor cells in the recipient. It is submitted that in order to overcome this compatibility issue, donor-recipient compatibility tests are conducted generally along with providing immunosuppressant drugs/therapy to suppress or reduce the strength of the recipient's immune system. Thus, a skilled person or a medical practitioner is well aware of the unpredictability, risks and safety issues if stem cells from one individual are transferred to another.

6. It is submitted that the advantage of the present invention can further be fortified by the fact that till date the Appellant has successfully obtained license and approval from the Drugs Controller General of India (DCGI) for the permission to manufacture and market the stem cell drug "Stempeucel®" (a pooled MSC product envisaged by the present application) for the treatment of Critical Limb Ischemia due to Buerger's disease. The Appellant stated that it has also obtained necessary approvals for clinical trials of said drug for other disease conditions as well.

7. It is submitted that the The enhanced immunosuppression activity of the pooled MSC composition and the successful approvals of the Stempeucel® (pooled MSC product) highlights the safety or compatibility of the product for practical applications in treatment of medical condition(s). The properties including enhanced angiogenic cytokine profile and enhanced chondro differentiation rate of the pooled MSC composition and the successful approvals of the Stempeucel® (pooled

MSC product) indicate the efficacy of the product for practical applications in treatment of medical condition(s). The Appellant's stem cell product Stempeucel® has also shown significant promise in the treatment of COVID-19 owing to the anti-inflammatory and immune-modulatory properties which prevents over-activation of the patient's immune system. Said product exhibits potent immune-modulatory and anti-inflammatory properties which could help in reducing the inflammation caused due to the cytokine storm elicited by the body's immune cells in response to SARS-CoV-2 (COVID-19) related infection in the lungs. Also, the growth factor, Angiopoietin-1 (Ang-1) is effective in reducing alveolar epithelium permeability in the lung permeability, thus, reducing fatal symptoms of COVID-19 induced pneumonia and progress to Acute respiratory distress syndrome (ARDS). The Appellant is currently in the process of receiving regulatory approvals for the same. Additional details on the utility and success of Stempeucel® is provided under paragraph numbers 4 to 8 (page numbers 2 to 4) and Annexure C (page numbers 11 to 16) of the Miscellaneous Petition No. 5 of 2020.

8. The Respondent has refused the grant of the present application for not meeting the requirements of paragraphs 1 to 3 (objections) of hearing notice dated September 10, 2014. Said objections are the following:

a) Objection 1: Proof of right: The Learned Respondent states that the proof of right was not filed within the time limit prescribed under Rule 10 of the Indian Patent Rules, 2003;

b) Objection 2: Section 3(e) – Mere admixture: The Learned Respondent states that the compositions (products) claimed in claims 11 and 12 are mere admixtures resulting in an aggregation of the properties of the components thereof without any synergistic effect and hence patent ineligible under Section 3(e).

c) Objection 3: Section 2(1)(ja) – Inventive Step: The Learned Respondent while acknowledging the noveltystates that the invention claimed in claims 1 to 12 describing methods and compositions is not inventive as per Section 2(1)(ja) of the Act.

9. Proof of right

It has come on record that all the 8 inventors mentioned in the present application were/are the employees of the Appellant. Five inventors were named in the 'Provisional Application' filed on November 27, 2009 and proof of right was timely filed on March 02, 2010 (well within the prescribed time-period of 6 months as per Rule 10). One of the inventors 'SatishMahadeoraoTotey' had left the services of Appellant and accordingly the Appellant had filed an Affidavit before the Respondent on March 02, 2010 to confirm the same, which is again well within a period of 6 months as contemplated under Rule 10. Three additional inventors were added in the 'Complete Application' filed on November 26, 2010 and proof of right for said additional inventors was also timely filed on December 31, 2010 (well within the prescribed time-period of 6 months as per Rule 10).

However, as appeared from the impugned order, the Respondent in the First Examination Report [FER] dated 28.11.2013 [Annexure A5) vide objection no. 4 raised an objection that *"Inventor in the Application Form -1 has not signed the declaration"*. To which the Appellant by its reply dated 05.02.2014 [Annexure A-6] re-submitted its earlier submissions dated March 02, 2010 and November 26, 2010. But, despite of that, the Respondent *vide* its Hearing Notice dated 10.09.2014 [Annexure A-2] raised an objection that *"an affidavit cannot meet the requirement of Section 7(2)"*.Since the Respondent was still adamant to get an Executed Form-1, the Appellant was able to reach out to the inventor, 'SatishMahadeoraoTotey', and got the Form-1 executed and submitted the

same before the Controller vide its response dated 18.12.2014 [Annexure A-10]. Despite the same, the Respondent has rejected the Application on the ground that that the proof of right was not filed within the time limit prescribed under Rule 10 of the Indian Patent Rules, 2003.

10. It is not in dispute that SatishMahadeoraoTotey left the service. As required under Rule-10, his affidavit was filed on 2.3.2010 after making best efforts by the appellant. Since the respondent was not satisfied, even he executed Form-1 because of objection raised and requirement under Section 7(2) of the Act.

11. It has come on record that after leaving the service, the appellant has not having any control on his where-about, but still the compliance is done once he was approached by the appellant. He has not taken any contrary stand. He in a way admitted that he was the employee of the appellant.

Delay, if happened, was beyond the control of the appellant. He is not claiming his independent right about the invention. It was a bonafide conduct of the appellant. Thus, the finding arrived by the respondent by taking the very harsh view.

12. The Impugned Order is thus against the fundamental principles of law pertaining to master and servant and that the rights are deemed assigned to the Employer/Appellant by virtue of relationship of employment of the inventor with the Appellant. The Appellant is relying on the decisions of The High Court of Justice—Chancery Division as passed in the matter of *Triplex Safety Glass Co. Ltd. v. Scorah*(1938 RPC Vol. LV Page 21) and decision of House of Lords as passed in the matter of *Patchett v. Sterling Engineering Co. Ltd.* (1955 RPC Vol. LXXII, at Page50) wherein Courts held *"that where the employee in the course of his*

employment (i.e. in his employer's time and with his material) makes an invention which falls within his dutyto make (as was the case here) he holds his interest in the invention and in any resulting patent as trustee for the employer unless he can show that he has a beneficial interest which the law recognizes".

13. Actually, it was on a persistent requirement from the Respondent, executed Form-1by the inventor, 'SatishMahadeoraoTotey'was submitted, but despite the same, the Respondent rejected the Present Application on the ground that that the proof of right was not filed within the time limit prescribed under Rule 10 of the Indian Patent Rules, 2003. Had he been working with the appellant, the position would have been different or he was easily approachable, but both elements are missing in the present case. It was beyond the control of the appellant to meet the requirement.

14. In this regard, Appellant is relying on the decision of this Board as passed in the matter of *NTT DoCoMo Inc. vs. The Controller of Patents and Designs*; Order No. 252 of 2013 wherein the Board duly recognized the importance of Proof of Right, however the Board went ahead and quashed the order of Ld. Controller which rejected the Application on the basis of non-compliance of Section 7(2) of the Act and allowed the Applicant to file necessary proof of right document. Said Application i.e. 794/CHE/2006under adjudication in Order No. 252 of 2013 stands granted as on date vide patent no. 259552.

15. In view of above, the Appellant despite having fulfilled the proof of right requirement, the Present Application was rejected.The same findings are not acceptable in view of reason explained by the appellant.

16. <u>Mere admixture</u>

Now, we will deal with the second objection about Section 3(e) of the Act. The Respondent in the impugned order has observed that the Applicants arguments is mainly for the specificities with which the method claimed can only be considered for novelty and the claims establish the novelty over the cited documents**.**Therefore, as per Respondent all the claims of the Present Application are NOVEL**.**

17. Section 3(e) states -

What are not inventions: The following are not inventions within the meaning of this Act:

> *……..“a<u>substance obtained by a mere admixture resulting only in the aggregation of the properties of the components thereof</u> or a process for producing such substance”.*

It is stated on behalf of appellant thatunderstanding on the said clause is provided by the ‘Guidelines for Examination of Biotechnology Applications for Patent’(hereinafter referred to as the “Guidelines”) issued by the Indian Patent Office, which at paragraph 10.12 states that when “*old integers placed together has some working interrelation producing a new or improved result, then there is patentable subject matter in the idea of the working inter relations brought about by the collocation of the integers*”. The Guidelines further clarify this by referring to ‘*Ram PratapVsBhaba Atomic Research Centre (1976) IPLR 28 at 35’*, and stating that “*…it was held that a mere juxtaposition of feature already known before the priority date which have been arbitrarily chosen* from *among a number of different combinations which could be chosen was not a patentable invention*”,

Further, Hon’ble High Court of Bombay in the matter of *LallubhaiChakubhaiJariwala vs. ChimanlalChunilal and Co.; AIR 1936 Bom 99* held that -

> *“<u>In the case of a combination the inventor may have taken a great many thingswhich are common knowledge and acted on</u>*

> *a number of principles which are well-known.If he has tried to see which of them when combined produce a new anduseful result, and if he succeeds in ascertaining that such a result is arrived at by aparticular combination, the combination will, generally speaking, afford subjectmatterfor a patent.*

Thus, it appears to us that the applicability of Section 3(e) is valid only in scenarios where a claimed product is obtained by combining known or already existing ingredients, and the burden of showcasing synergistic effect for such product is therefore necessary. Meaning thereby, a product or composition comprising a novel ingredientcannot fall under the ambit of Section 3(e) of the Act.The legislative intent behind Section 3(e) of the Act can further be traced in the Judgment by Hon'ble Supreme Court of India as passed in the matter of *Novartis AG vs Union of India & Others*; *CIVIL APPEAL Nos. 2706-2716 OF 2013* wherein it has been held at paragraph 92 that:

> *"The Chapter has the Heading "Inventions Not Patentable" andsection 3 has the marginal heading "What are not inventions." As suggested by the Chapterheading and the marginal heading of section 3, and as may be seen simply by goingthrough section 3,* ***it puts at one place provisions of two different kinds: one that declaresthat certain things shall not be deemed to be "inventions" [for instance clauses (d) & (e)];****and the other that provides that, though resulting from invention, something may yet not begranted patent for other considerations [for instance clause (b)]."*

18. Thus, it is settled that most invention are a combination of old elements. The mere existence in the prior arts of each of the elements will not ipso facto means that the invention offend under section 3€ of the Act.

19. We agree with the submissions made on behalf of appellant that applicability of Section 3(e) cannot be looked from the prism of assessing novelty and inventiveness but same has to be looked from the perspective of matter of policy. Further, it shall be applicable only when a claimed

product is obtained by combining known or already existing ingredients, and not when integers of the claimed product is itself not known.

20. In the present case, the appellant claimed compositions of claims 11 and 12 comprise pooled MSCs – an ingredient/feature which is novelas admitted by the Respondent. The Respondent has misconstrued the provisions of Section 3(e) of the Act and has contradicted by acknowledging the claims 11 and 12 as novel on one hand, and rejecting the same compositions claims 11 and 12 for lack of synergistic or improved effect data, on the other. By virtue of the compositions of claims 11 and 12 comprising a novel ingredient (pooled MSCs), Section 3(e) for said claims does not apply.SinceSection 3(e) is not applicable to the present application.However, the Appellant in order to satisfy the respondent experimental results (discussed hereinbelow) highlighted. That the pooled MSCs *per se*inherently showcasestechnical advancement over un-pooled MSCs *per se*. Thus, the composition of pooled MSCs claimed under claims 11 and 12 of the present application is novel and inventive and synergistic interplay of pooled MSCs and other components of the compositions of claim 11 and 12 thereby showing enhanced viability, which is not seen when: a) pooled MSCs are combined with individual components of the composition of claims 11 and 12; *and* b) when pooled MSCs and other components are at concentrations beyond the ranges recited in claim 11.

In view thereof, we are of the view that the objection raised by the respondent is not sustainable and is waived accordingly.

INVENTIVE STEP:

21. We shall now deal with the third objection raised by the respondent. The appellant claimed that the compositions of the present application comprising pooled MSCs provide following technical advantages over single donor MSCs (Prior Art):

a) enhanced chondrodifferentiation potential (i.e. enhanced growth potentialto generatecartilage cells – a specific cell type of the body),

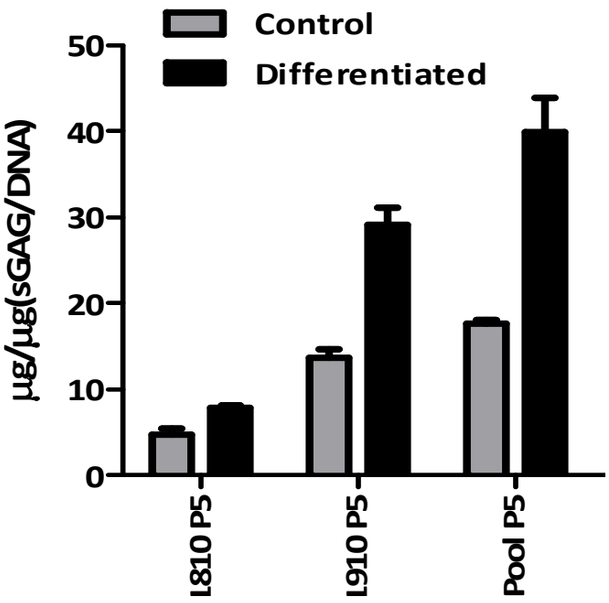
b) enhanced cytokine (growth factor) profile,

c) enhanced immunosuppression (immunomodulatory property),

d) a homogenous and consistent MSC product with enhanced cell viability.

It was claimed that the above-mentioned technical advantages highlight the superiority/technical advancement along with synergistic effects of the compositions comprising *pooled* MSCs over single donor MSCs. Said technical advantages were provided to the Respondent *vide*Response dated 18.12.2014 to Hearing Notice**.** For the benefit of this Board, said technical advantages are demonstratedand detailed at page numbers 634 to 642and is summarized below:-

a) <u>Enhanced Chondro differentiation potential</u>

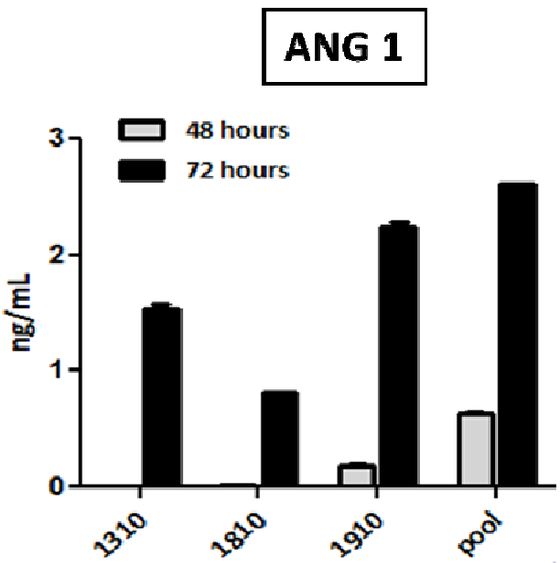


This experiment measures the ability of MSCs to give rise to cartilage cells (chondrocytes). Said ability can be determined by measuring sulphated glycosaminoglycan (sGAG) levels which is a molecule secreted by chondrocytes. Hence, greater the sGAG quantity, better is the chondro

differentiation potential of the product. 1810 P5 and 1910 P5 are single donor MSCs (prior art) and Pool P5 is pooled MSCs (present application).

Results/Conclusion: There is about 80.5% increase in the chondrodifferentiation rate of pooled MSCs (pool P5) compared to single donor MSC 1810P5 and about 27.2% increasecompared to single donor MSC 1910 P5. The results demonstrate that compositions comprising pooled MSCs have enhanced chondro-differentiation rate compared to single donor MSCs.

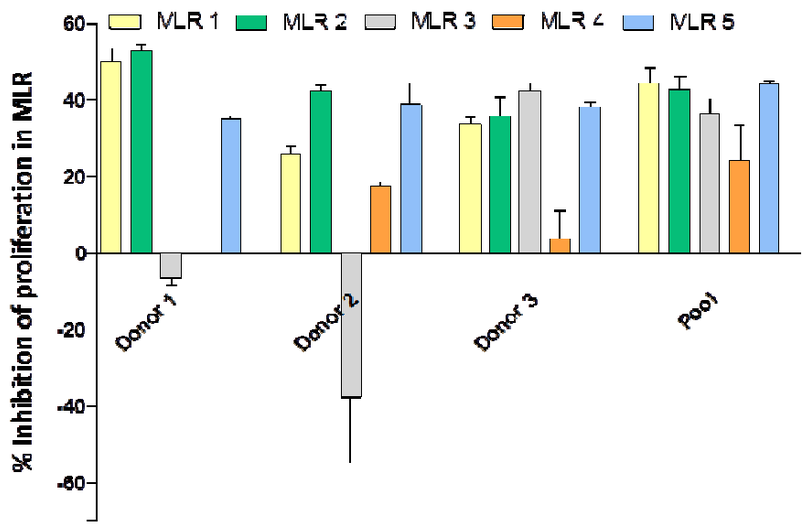
b) Enhanced Angiogenic Cytokine profile



This experiment measures Angiogenic Cytokine (Ang-1 or Angiopoietin 1)content which is one of the most important growth factorsrequired for the stabilization of blood vessels.1310, 1810 and 1910 are single donor MSCs (prior art) and Pool is pooled MSCs (present application).

Results/Conclusion: At 72 hours, there is about44.3% increaseof Ang-1 in pool compared 1310, about 69.3% increasecompared to 1810 and about 15.4% increasecomparedto 1910. The results clearly demonstrate that compositions comprising pooled MSCs show enhanced Angiogenic Cytokine (Ang-1) secretion compared to single donor MSCs.

c) Enhanced Immunosuppression Activity



This experiment tested the ability of MSC products to inhibit or reduce Mixed Lymphocyte Reaction (MLR). Mixed lymphocyte reaction (MLR) is a test used to show the safety or compatibility of a drug product.Greater the ability to inhibit MLR (i.e. % inhibition of proliferation in MLR), more compatible is the product for therapeutic use. Donor 1, Donor 2and Donor 3 are single donor MSCs (prior art) and Pool is pooled MSCs (present application).

Results/Conclusion: Individual donors depict considerable variation in the inhibition of MLR, sometimes also being unable to inhibit a particular MLR (*see*Donor 1 and Donor 2 which are unable to inhibit MLR 3).On the contrary, composition comprising pooled MSCs (pool) showconsistent inhibition ofproliferationacross all MLR types (MLR 1, MLR 2, MLR 3, MLR 4 and MLR 5)indicating better immunosuppression activity.

d) Enhanced Cell Viability and Synergy

(i) Effect of varying concentrations of ingredients

Sample Formulation Study				
Vials	Test	**Formulation 1A**	**Formulation 4**	**Formulation 5**
1	Viability	**84.30%**	35.30%	79.50%
2	Viability	**85.50%**	38.30%	77.80%

3 (i)	Viability	**86.40%**	34.00%	76.70%

) Table 1: Cell viability of composition of Claim 11

[7-aminoactinomycin D (7AAD) test]

This experiment tested the effect of cell viability based on the varying concentrations of the ingredients described in thecomposition of Claim 11. Cell viability of the composition of claim 11 (referred as Formulation 1A) was compared with cell viability ofsimilar compositions (referred as Formulation 4 and Formulation 5) wherein the concentrations of components, DMSO, HSA and MultipleElectrolytes Injection, Type 1 USP, were varied outside the ranges provided in claim 11.

Sample Formulation Study				
Vials	Test	**Formulation 1B**	**Formulation 2**	**Formulation 3**
1	Viability	**93.64%**	89.88%	62.74%
2	Viability	**92.22%**	84.84%	63.93%
3	Viability	**97.48%**	88.45%	61.79%

Table 2: Cell viability of composition of Claim 12

[7-aminoactinomycin D (7AAD) test]

This experiment tested the effect of cell viability based on the varying concentrations of the ingredients described in the composition of Claim 12. Cellviability of the composition of claim 12 (referred as Formulation 1B) was compared with cell viability of similar compositions (referred as Formulation 2 and Formulation 3) wherein the concentrations of components, DMSO, HSA, and Multiple Electrolytes Injection, Type 1 USP, were varied outside the ranges provided in claim 12.

Results/Conclusion: The viability of Formulation 1A (i.e. composition of claim 11) was about 85.4% (average), whereas the viability of Formulation 4 and Formulation 5 (comparative compositions) were about35.8% (average) and about 77.9% (average).

The viability of Formulation 1B (i.e. composition of claim 12) was about 94.4% (average), whereas the viability of Formulation 2 and Formulation 3 (comparative compositions) were about 87.7% (average) and about 62.82% (average).

22. It appears that the above results show that the compositions of claim 11 and claim 12 have enhanced viability when compared to compositions of MSCs having the same components with concentrations falling outside the concentration ranges described in claims 11 and 12.

23. The appellant was also able to show the results additionally the synergistic interaction of concentrations of different ingredients within theclaimed compositions to provide improved cell viability.

(ii) Effect of varying ingredients:

Percentage Viability	Trypan Blue test			7AAD test (see Figure 1)		
	Vial 1	Vial 2	Vial 3	Vial 1	Vial 2	Vial 3
MSC+ Freeze Mix	**100**	**100**	**100**	**88.8**	**90.6**	**87.2**
MSC+HSA	57.2	39.2	69	31.2	27.6	31.2
MSC+DMSO	0	0	0	14.5	13.5	13.4
MSC+PLA	0	0	0	10.1	10.5	10.5

Table 3: Percentage cell viability

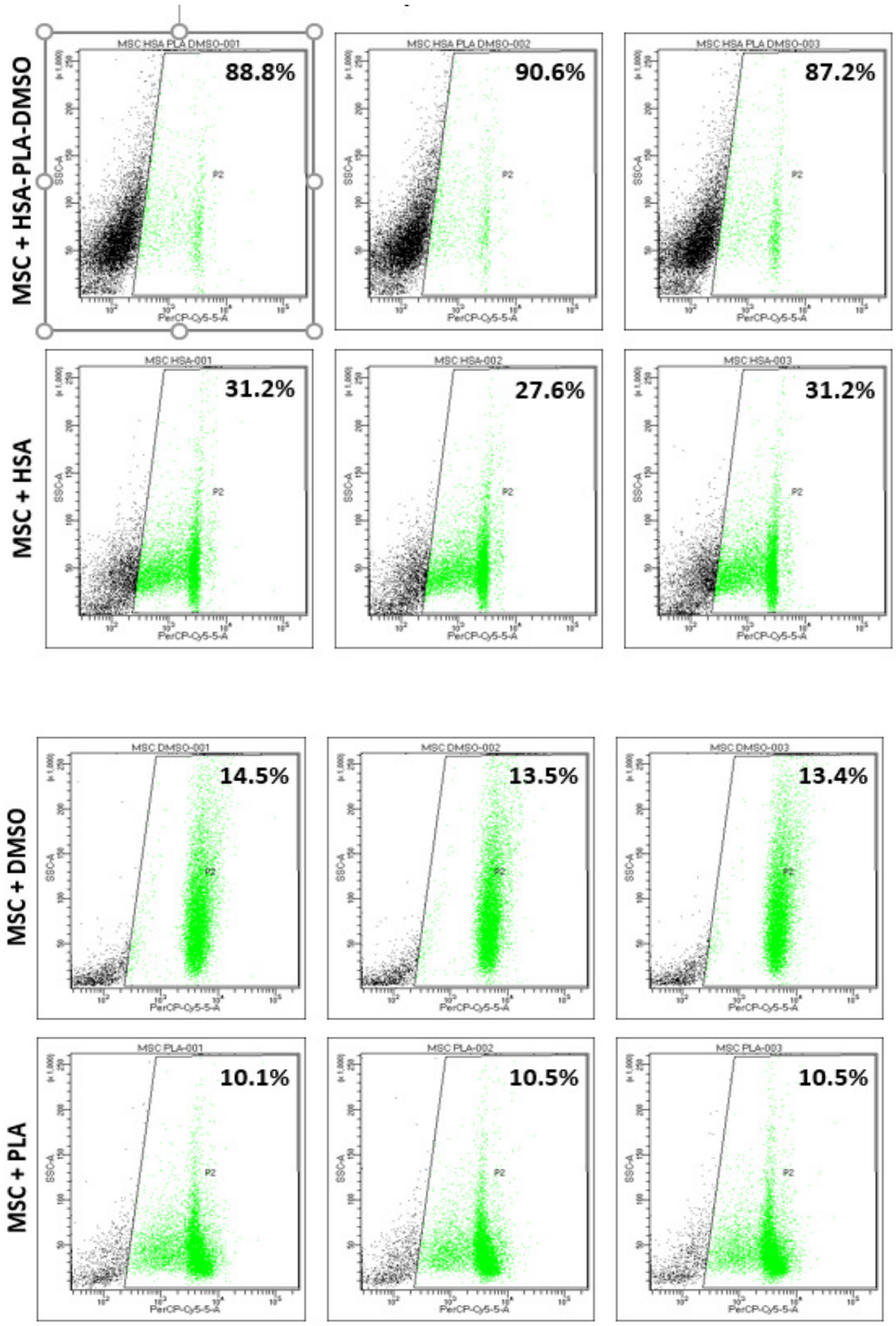


Figure 1: Percentage cell viability [7-aminoactinomycin D (7AAD) test]

Theabove experimentsunder Table 3 and Figure 1describe cell viability tests of the claimed composition comprising pooled MSCs in combination with all ingredients provided in Claim 11 versus cell viability of compositions comprising pooled MSCs with each of the said ingredients individually. The compositions employed in the experiments were as follows:

- MSC + Freeze Mix *or* MSC + HSA-PLA-DMSO: Composition of claim 11

- MSC + HSA: Comparative composition comprising pooled MSCs and human serum albumin (HSA)

- MSC + DMSO: Comparative composition comprising pooled MSCs and dimethyl sulfoxide (DMSO)

- MSC + PLA: Comparative composition comprising pooled MSCs and Multiple electrolytes injection, type 1 USP, (PLA)

Results/Conclusion: As seen from Table 3, the percentage cell viability of the composition of claim 11 is enhancedcompared to the cell viability of MSCs when combined with the individual components such as DMSO, HSA or multiple electrolytes injection, Type 1 USP. These results clearly showcase the synergistic interplaybetween all the ingredients within the composition of the present application leading to improved cell viability which is absent when the MSCs are combined with individual ingredients.

24. Despite the afore-mentioned results already submitted before the Respondent, the Respondent rejected the Present Application on the ground that *"the optimization of the specific parameter and ingredient concentration is routine experimentation practice and which do not involve any inventive ingenuity"*, hence the compositions and methods of the present application are not inventive over the cited prior art documents D1 (*Darwin J. Prockop, Donald G. Phinney, Bruce A. Bunnell. Mesenchymal stem cells, and protocols. Humana press.2008. Chapter 2- Mesenchymal stem cells from Adult Bone Marrow*), [Annexure A-7]; D2 (*Rakhi Pal, MadhuriHanwate and Satish M. Totey.Effect of holding time, temperature and different parenteral solution on viability and functionality of adult bone marrow-derived mesenchymal stem cells before transplantation.Journal of Tissue Engineering and Regenerative Medicine. Volume 2, Issue 7, Pages 436-444, October, 2008*) [Annexure A-8] and D3 (*WO2007084354*)[Annexure A-9].

25. It is submitted on behalf of appellant that the prior art provides products (compositions) containing single donor MSCs i.e. un-pooled MSCs, and methods for preparing such un-pooled MSC products.More particularly, D1 describes isolating MSCs from adult bone marrow, their expansion and multilineage differentiation.More particularly, from **D1 a** person skilled in the art can arrive at the teachingof addition of FBS and DMSO + single donor/un-pooled MSCs. D2 describes effect of holding time, temperature and different parenteral solutions on viability and functionality of adult bone marrow-derived mesenchymal stem cells.More particularly, from **D2 a** person skilled in the art can arrive at the teaching of harvested single donor/un-pooled MSCs + Multiple electrolytes injection, type 1 USP. D3 discloses method of treating genetic disease(s)by employing mesenchymal stem cells. More particularly, from **D3 a** person skilled in the art can arrive at the teaching of single donor/un-pooled MSCs + HSA, DMSO and Multiple electrolytes injection, type 1 USP. Additional details on D1, D2 and D3 and their differences/non-obvious features *vis-à-vis* present application are provided under paragraph 5.11 (i. to xxxviii) at ink page numbers 000013 to 000029of the Statement of Appeal dated April 07, 2017.

25.1 None of the documents D1 to D3individually or in combination teach or motivate to perform pooling of MSCsof multiple donors to arrive at a pooled MSC product. Said teachings of D1 to D3 solely focus on MSCs from single donor, followed by further processing of such single donor MSCs without hinting or even remotely suggesting that pooling of MSCs from multiple donors could even be an option.

25.2. It is a known fact that the mesenchymal stem cell products or drugs are *not* commonly/widely employed for treatment of medical conditions and said practical applications of stem cells as therapeutic products is still

a developing area. That the feature of pooling of MSCs to prepare a therapeutic pooled MSC product is additionally difficult to envisage by a skilled person/medical practitioner since the concept of injecting foreign MSCs (single donor MSCs) to a subject is itself unpredictable and challenging due to the compatibility issues and risks associated with the same as discussed above in detail.

25.3 D3 at Example 1of D3 (page number 412, first paragraph) states that *"…increased donor MSC persistence can be achieved by reducing the host MSC population through the use of full body irradiation and/or chemoblative or nonblative procedures before donor MSC delivery to patient". The said excerpt of D3 further demonstrates the well-established issue of compatibility and associated riskswhen injecting MSCs of a different individual (donor MSCs) to a patient.In particular, D3 teaches reducing or removal of the own MSCs of the patient before administration of donor MSCs to said patient.*

25.4 The general knowledge of a skilled person on compatibility issues and associated risks by injecting donor cells to a patient is well understood. The same is even more pertinent from prior art document such as D3 which clearly motivates a skilled person or medical practitioner to try and avoid injecting MSCs, let alone injecting pooled MSCs.

26. The Appellant has relied upon the decision of Hon'ble High Court of Delhi as passed in the matter of *Bristol-Myers Squibb Holdings Ireland Unlimited Company &Ors. vs BDR Pharmaceuticals International Pvt. Ltd. &Anr.; CS(COMM) 27/2020*wherein it has been categorically held that:

> *38. As noted above, <u>it is thus well settled that in case prior art document show a concept of teaching away from the inventive step, the said prior art document cannot be used to demonstrate that the invention is obvious and thus not liable to be patented</u>.*

In the said judgment *(supra)*, the Hon'ble Court laid down the following principles which govern the field to find out whether an invention is obvious or not, and can be summed up as under: -

i. *A hindsight reconstruction by using the patent in question as a guide through the maze of prior art references in the right way so as to achieve the result of the claim in the suit, is required to be avoided.*

ii. *The patent challenger must demonstrate the selection of a lead compound based on its promising useful properties and not a hindsight driven search for structurally similar compounds.*

iii. *There should be no teachings away from the patent in question in the prior art.*

iv. *Mere structural similarity cannot form the basis of selection of lead compound in a prior art and the structural similarity in the prior art document must give reason or motivation to make the claim composition.*

v. *Though mosaic of prior art documents may be done in order to claim obviousness, however, in doing so, the party claiming obviousness must be able to demonstrate not only the prior art exists but how the person of ordinary skill in the art would have been led to combine the relevant components from the mosaic of prior art.*

vi. *It has to be borne in mind, small changes in structures can have unpredictable pharmacological effects and thus, structural similarity alone is not sufficient to motivate to selection of the lead compound.*

vii. *Though it would be tempting to put together a combination of prior arts but this requires a significant degree of hindsight, both in selection of relevant disclosures from these documents and also in disregarding the irrelevant or unhelpful teachings in them.*

27. The said decision goes in favour of the submission made on behalf of appellant that the general art and the disclosure of cited document D3 alone or in combination with D1/D2 clearly teach away from the critical concept/feature of the present application (claims 1-12)i.e. pooled MSCs. The concept/method of pooling MSCs from multiple donors to develop a therapeutic pooled MSC product is unheard and unforeseen in the prior art.Said pooled MSC product further shows surprising/unexpected technical effectsover prior art (un-pooled MSC product) as discussed above. The Appellant has also shown that the pooled MSC product of the present application possess enhanced chondro differentiation potential, enhanced cytokine (growth factor) profile,enhanced immune suppression,a homogenous and consistent feature with enhanced cell viability suitable for therapeutic use. Said improved technical effects indicate the safety, compatibility and efficacy of the pooled MSC products and methods of the present application.

28. It is rightly alleged by the learned counsel that when the compositions themselves are not envisaged by the prior art,arrivingat the methods to prepare such unknown compositionsis even more far-fetched for a person skilled in the art.It is pertinent to mention that methods cannot be randomly designed to pool MSCs – when there is no motivation from or teaching in the prior art on how to combine MSCs. A person skilled cannot randomly introduce a method step of pooling and expect the final product to work and give technically advanced solutions, especially in situation when the artitself teaches away from the critical concept/feature of the present application (claims 1-12)i.e. pooled MSCs.On the contrary, such a random introduction of mixing step might cause the cells to die or give rise to negative interactions, as under normal circumstances, cells from one donor are not meant to interact with cells from another donor, let alone from three other donors. Hence, inventive ingenuity needs to be kept in mind while designing methods to pool the cells for desired/beneficial

final product, which the inventors in the present case have been able to achieve. Therefore, the compositions and methodsdescribed in claims 1 to 12 of the present application are non-obvious/inventive over cited documents D1-D3. It is also a matter of fact that despite of service of appeal, no counter-affidavit has been filed by the respondent. The grounds raised have gone un-rebutted. There was a representation on behalf of respondent.

29. It is also a matter of fact that the present application with similar claimscope is granted in 18 countries. Following is a compilation summarizing the countries, statusof foreign applications.

Sl. No.	**Corresponding Country**	**Application No.**	**Status**
1	Australia	2010325546	Granted
2	Canada	2,777,232	Granted
3	China	201080053627.3	Granted
4	Malaysia	PI 2011000552	Granted
5	New Zealand	599407	Granted
6	South Africa	2012/02685	Granted
7	Singapore	201202664-7	Granted
8	Vietnam	2-2012-00093	Granted
9	Indonesia	W-00 2012 02048	Granted
10	Philippines	1-2012-500892	Granted
11	Europe	10832735.4	Granted
12	Japan	2015-64305	Granted
13	Japan	2012-540529	Granted
14	United States of America	13/062,189	Granted
15	France	2504426	Granted (EP Validated)
16	Germany	60 2010 036 848.3	Granted (EP Validated)
17	Italy	2504426	Granted (EP Validated)
18	United Kingdom	2504426	Granted (EP Validated)

30. One of the features of the Patents Amendment Act, 2002 was to define the term "invention" in consonance with international practices and consistent with TRIPS Agreement.

The definition of "new invention" was widened where it allows any invention or technology which has not been anticipated by the publication in any document or used in the country or elsewhere in the world before the date of filing of patent application with complete specification, i.e. the subject matter has not fallen in public domain or that it does not form part of the state of the art.

31. The Objects and Reasons of the Patents Amendment Act, 2005 states that

> *While considering the third set of amendments to the Act, efforts have been made not only to fulfil our final obligation under the TRIPS Agreement,* ***but also to simplify and rationalize the procedure governing grant of patents so as to make the system more efficient and User friendly****.*

32. Hence, it is clear that amendments in the Act till 2005, was made to bring the Patents Act of India, not only in consistent with TRIPS Agreement but also to make it in consonance with international practices. In a way it would be prudent to suggest that the Act makes an attempt to consider that tests of novelty and obviousness are universal in nature.

33. Hon'ble High Court of Delhi in the matter of *Communication Components Antenna Inc. vs Ace Technologies Corp. and Ors.* beautifully captured the following:

> *34. In order to appreciate the effect of statements made during prosecution of patents internationally and in India, it is necessary to state the prevalent patent prosecution practices.*
>
> *35. It is a matter of common knowledge that whenever applications are filed through the PCT route, the international filing office for PCT applications, which is run and managed by the WIPO, issues an "International Search Report" (hereinafter, "ISR"). Along with the ISR, the WIPO also issues an International Preliminary Examination Report ("IPER"), if a request in this behalf is made by the applicant. If no request is made by the applicant, then the WIPO issues a report called International Preliminary Report on Patentability ("IPRP"). The*

details contained in the IPER are the same as those in the IPRP. This ISR, along with the IPER or the IPRP, as the case may be, primarily gives a direction, on the basis of the initial search done by the WIPO, as to whether the invention disclosed is novel and inventive and whether a patent is likely to be granted or not. Depending on the opinion in the ISR and IPER/IPRP, the applicant chooses to move the patent application from the international phase into the domestic phase of countries where the applicant feels that it is likely to get a patent.

36. Prosecution of patents is an expensive exercise and thus, the facility of ISR with IPER/IPRP, enables an applicant to take a considered decision on the likely grant of the patent in a particular jurisdiction. This eliminates unnecessary expenses incurred by applicants in prosecuting applications in various countries, across the world. The ISR, along with its supporting documents, is based on an initial search conducted on major patent databases, by the international filing office. Thus, the search reports issued by the PCT office are to be treated like a first filter rather than a conclusive opinion on patentability.

37. Once the patent application enters the domestic phase, various national patent offices examine the application in terms of the substantive and procedural laws of the respective country. Patent rights are territorial in nature and are limited to the country of grant. Broadly speaking, in order for grant of a patent, the three tests of novelty, inventive step and industrial applicability have to be satisfied. However, there are several nuanced and intricate dimensions to these three tests, in each and every jurisdiction. Apart from the substantive law of a country, the patent prosecution practices of various patent offices are also different. Finally, the subjective satisfaction of each patent examiner in a jurisdiction would also be different. Thus, there is a four-step analysis/processing of an international patent application filed through the PCT route viz.,

(i) International Search Report stage (ISR/IPER/IPRP);
(ii) Examination as per substantive laws in the domestic phase in each country;
(iii) Examination as per guidelines, patent prosecution practices and other procedural laws and
(iv) Subjective satisfaction of the examiner during the examination process.

38. While patent applicants ought to be held bound by the broad statements made during prosecution of their patents in various jurisdictions, there is bound to be differences in the wording of claims which may happen. When a patent application undergoes issuance of examination reports and replies being filed thereto, the applicant makes various statements in order to overcome objections raised during examination. These statements are sometimes substantive in nature, and sometimes are merely clarificatory in nature. Deletion of a claim, for e.g., to overcome the objection of a prior art, would be a substantive change. Adding or deleting language within a claim may also be clarificatory in nature. Sometimes examiners are convinced with one type of wording rather than the other and it is usual for patent agents and applicants to defer to the examiner's viewpoint. The culture of patent offices in wording of claims varies from country to country. In each and every case therefore, the statements made during prosecution of either the subject patent, or corresponding patents internationally, need to be seen in order to arrive at a conclusion as to what is the effect of the said statement on the extent of monopoly enjoyed, which is governed by the claims of the patent.

41. The language of the claims in different jurisdictions of the same convention application after it is granted in the various domestic jurisdictions, would usually never be identical. This is due to the subjectivity that exists in the prosecution process of the application, as discussed above……
Insofar as an Indian Court are concerned, while determining the question of validity of a patent, it would be concerned primarily with the claims that have been granted in India. The unique nature of grant of patents in various jurisdictions or the wording of claims in various jurisdictions would only have a broad impact on the Indian claims, and not more.

34. It is true that the International Search Report (ISR) issued by World Intellectual Property Organization in respect of PCT application is not binding in view of Article 33(1) of the Patent Cooperation Treaty, which provides that the object of the International Preliminary Examination is to formulate a preliminary and non- binding opinion. Article 35(2) of the PCT provides that the International Preliminary Examination Report shall not contain any statement on the question whether the claimed innovation is patentable or not according to any national law. But we are of the view that some importance is to be given when the similar patent in many other countries are registered after overcoming the objection of prior art, novelty, obviousness. It may not be binding effect but the Examiner must take into this aspect while examination of application and to consider alsoabout the registration of some invention in other countries at the time of raising objection in the examiner report.

Thus as per *Ten Xc Wireless Inc and Another v. Mobi Antenna Technologies*, [2012] 187 DLT 632, the findings of the ISR and IPRP are not binding on the Indian Patent Office, and cannot override the provisions of the Act especially on issues of novelty and inventiveness. Reference to Sections 13(1) and (2) of the Act indicate that the duties set out therein for the concerned Examiner are mandatory, in view of use of the term "shall" in both provisions. It is therefore inconceivable that the statutory duties of the concerned Examiner to conduct a prior art search can be set aside or circumvented by reliance on the findings of the ISR and IPRP.

35. The Madras High Court in the matter of *R. Muralidharan vs. The Controller General Of Patents*; W.P.No.33021 of 2014, held that

"……..PCT Search Report is being and shall be treated as an essential input in the examination by the Examiner, in pursuance of the mandate of Section 12 of the Patents Act, 1970 dealing with the question of examination of application."

36. The question is what would be happen if the claims rejected by the IPO is identical to the granted claims in major jurisdictions like EPO, USPTO and the rejection in India has happened on the basis of identical set of prior arts over which other jurisdictions have already granted patent.

37. No doubt, we agree if cited prior arts by the IPO are different from the cited prior arts in USPTO, EPO it may be justified that IPO has done its examination as per the provision but in the situation where identical claims are granted in major jurisdiction and still such patent claims are rejected in India, the same may be in contradiction to the statements and objects of the Patents Amendment Act, 2005. It amounts to injustice and against the principles of equity and fair play.

38. In the light of above, we are of the view that the rejection of the Application, based upon the fact that executed Form 1 by one of the inventors namely SatishMahadeoraoToteywas not filed within 6 months as prescribed under Rule 10 of the Patent Rules, 2003,is wrong as due compliance was made. The said findings were against the fundamental principles of law pertaining to master and servant especially when executed Form 1 by one of the inventors namely SatishMahadeoraoToteywas already filed before the Respondent in addition to the declaration by way of an Affidavit which was duly filed within 6 months as prescribed under Rule 10 of the Patent Rules, 2003.

39. The rejection of the Application on the basis ofapplicability of Section 3(e) is not as per law.Section 3(e) shall be applicable only when a claimed product is obtained by combining known or already existing ingredients.

40. The rejection of the Present Application on the ground that the same is obvious in view of D1 to D3 is incorrect, as general art and the

disclosure of cited document D3 alone or in combination with D1/D2 clearly teach away from the critical concept/feature of the present application (claims 1-12)i.e. pooled MSCs.

41. In the light of above, the Impugned Order is set-aside by allowing the present appeal.

42. The Assistant Controller, Patents & Designs, New Delhi, is hereby directed to grant Patent as claimed by the appellant and proceed with the application as per rules.

43. No costs.

-Sd/- **-Sd/-**

(Dr. Onkar Nath Singh)
Technical Member (PVPAT)

(Justice Manmohan Singh)
Chairman