

Electronic Acknowledgement Receipt	
EFS ID:	36432650
Application Number:	15673316
International Application Number:	
Confirmation Number:	8074
Title of Invention:	METHOD FOR CONTROLLING RUST
First Named Inventor/Applicant Name:	Gilson Aparecido Hermenegildo de OLIVEIRA
Customer Number:	159570
Filer:	Parithosh Kumar Tungaturthi
Filer Authorized By:	
Attorney Docket Number:	UPL-005US
Receipt Date:	27-JUN-2019
Filing Date:	09-AUG-2017
Time Stamp:	14:50:06
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
------------------------	----

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Amendment/Req. Reconsideration-After Non-Final Reject	UPL-005-US_Tridium-Copper_Resp-NFOA-dtd-31Dec2018.pdf	247806	no	13
			de4115f52d1bfa8fb0181d2ba6cb43193dd9140a1		

Warnings:

Information:					
2	Affidavit-traversing rejectns or objectns rule 132	UPL-005-US_Declaration- under-132.pdf	4821706	no	14
			4dadc07f980e649f4506dfe13c0006ed223 aca0		
Warnings:					
The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing					
Information:					
3	Petition for review by the Office of Petitions	UPL-005-US_Petition-for- extension-of-time.pdf	185840	no	2
			317b27318c91ce97149d0982e3de50cf22c a6feb		
Warnings:					
Information:					
Total Files Size (in bytes):			5255352		
This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503. <u>New Applications Under 35 U.S.C. 111</u> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application. <u>National Stage of an International Application under 35 U.S.C. 371</u> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course. <u>New International Application Filed with the USPTO as a Receiving Office</u> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.					

UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor: OLIVEIRA, Gilson Confirmation No.: 8074

Aparecido Hermenegildo de

U.S. Patent Appl. No.: 15/673,316

Examiner: WANG, Shengjun

Filing Date: August 9, 2017

Art Unit: 1627

For: A method for controlling rust

Attorney Docket No.: UPL-005-US

DECLARATION PURSUANT TO 37 C.F.R. § 1.132

I, Dr. Gilson Aparecido Hermenegildo de Oliveira, do hereby declare and say as follows:

1. My resume is enclosed herewith, and being one of the inventors of the present application, I am competent to depose this declaration.
2. I am one of the 3 listed inventors for U.S. Patent Application number 15/673,316.
3. In order to describe the state of the art at the time of filing of the above application, and a long felt need for a fungicidal combination as disclosed in the application and recited in the currently pending claims, I provide the following:
4. The application, as originally filed, discloses triple combination of triple fungicides comprising at least one copper fungicide, at least one succinate dehydrogenase inhibitor fungicide, and at least one quinone outside inhibitor fungicide or at least one demethylation inhibitor fungicide, and the use of such combination in treating soybean rust. As such, the application is directed to a fungicidal combination comprising a multi-

site contact fungicide (copper fungicides) and two systemic fungicides (succinate dehydrogenase inhibitor, quinone outside inhibitor fungicide, and/or demethylation inhibitor). The pending claims are directed to the triple combination of fungicides and the use of such combination in treating soybean rust.

5. Soybean rust, also referred to as Asian soybean rust is caused by *Phakopsora pachyrhizi* and is an aggressive pathogen that was first detected in the U.S. in the fall of 2004. Since then to the time of filing of the instant application, it had spread from Asia to, at least, Africa, South America, and the U.S. Yield losses were estimated to be severe with this disease and almost 10-80% have been reported. Despite significant efforts to sustain soybean rust, it has been a record problem for soybean growers in the southeastern United States.
6. The control of soybean rust is a major concern for soybean producers. For example, soybean rust-mediated yield losses between 60% and 100% were reported in Brazil, Paraguay, and South Africa during the early 2000s. *Yorinori, J.T. et al., Epidemics of soybean rust (Phakopsora pachyrhizi) in Brazil and Paraguay from 2001 to 2003. Plant Dis. 2005, 89, 675-677.*
7. Yield losses estimated at 25% were first reported from commercial fields in Mississippi in 2009. *Allen, T.W. et al., A continuing saga: soybean rust in the continental United States, 2004 to 2013. Outlooks Pest Manag. 2014, 25, 167-174.*
8. "Starting with the 2003/2004 soybean production season, economic losses due to the disease (including costs of control) have been estimated at more than \$2 billion annually. *Scherm et al., Crop Protection. 28 (2009) 774-782.*



9. In 2012, soybean rust reduced yield by over 60% in > 200 ha in Alabama. **Sikora, E.J. et al., Observations on soybean rust management in Alabama in 2012. In Proceedings of the Southern Soybean Disease Workers 40th Annual Meeting, Pensacola Beach, FL, USA, 13–14 March 2013.**
10. Since from 2001/2002 crop season to 2011/2012 crop season, the amount spent in controlling soybean rust increased from USD 177 million to USD 1.73 billion. **Godoy, C.V. et al., Asian soybean rust in Brazil: Past, present and future. Pesquisa Agropecuária Brasileira. 2016, 51(5):407–421. See Table 1.** The disease was estimated to cause yield losses of up to 90%. The importance of soybean rust was very evident in the industry, judged by its rapid expansion, virulence, and amount of losses. These are also highlighted in Dr. Godoy's study estimating grain losses and costs due to Asian soybean rust control. *Id.*
11. Fungicides most commonly used for soybean rust management, until publication of the instant application, were typically divided into two classes: demethylation inhibitors (DMI) and quinone outside inhibitors (QoI). DMI and QoI fungicides are locally systemic, meaning that they are taken up by the leaves and move within the leaf but not necessarily from leaf to leaf. Several DMI and QoI fungicides, including 6 triazoles, 2 strobilurins, 5 triazoles + strobilurins and 1 triazole + benzimidazole have been in use for Soybean rust control. Since the first fungicides emergency recommended for the 2002/03 season (azoxystrobin, difenoconazole, fluconazole, pyraclostrobin + epoxiconazole, and tebuconazole), many new formulations were added to the arsenal to control rust. Sensitivity monitoring tests by various groups in the industry revealed that the efficacy of the fungicides has been decreasing significantly over the years.



12. Research shows a clear trend towards decreasing efficacy of fungicides in controlling soybean rust severity or increasing yield in 2013, when compared with 2006 or 2007. *Id.*

13. Studies conducted by Dr. Cláudia Vieira Godoy, a renowned and highly published scientist in the field of fungicidal combinations, including specifically soybean rust control established a gradual decay in the efficacy of strobilurins, or conazoles or their mixtures towards the control of soybean rust, with their use, gradually over the years. ***Cláudia Vieira Godoy, Risk and Management of Fungicide Resistance in the Asian Soybean Rust Fungus Phakospora pachyrhizi, Fungicide Resistance in Crop Protection: Risk and Management (ed. T.S. Thind) CAB International 2012.*** "Combinations of strobilurins with triazoles improved disease and yield loss control compared with either class alone ... the reduced performance of triazoles observed 7 years after the introduction of *P. pachyrhizi* in Brazil, it reached a level at which rust control with straight azoles became unsatisfactory. Since 2007, the use of straight azoles has been decreasing and the use of triazole–strobilurin mixtures was intensified as the major strategy to reduce the risk of resistance." *Id.* However, the combination of such triazole and strobilurin did not provide a consistent soybean rust control, tested from 2006/07 to 2009/10. *Id.* Further, the studies show a decrease in the efficacy of the combination of triazole and strobilurin after use over a few years. *Id.*

14. A review article presenting a meta-analytical synthesis of the results of 71 uniform fungicide trials containing 930 specific fungicide treatments for the control of soybean rust, and yet concluded that combinations of strobilurins with triazoles was the best treatment available in the industry. ***Scherm, H. et al., Quantitative review of fungicide efficacy trials for managing soybean rust in Brazil. Crop Protection. 2009, 28, 774-782.*** Later, evidence showed that even the efficacy of this best possible treatment by combinations of

07

strobilurins with triazoles was seen to be decaying with gradual decay over the years. *Id.*
"Combinations of triazoles with a benzimidazole fungicide did not improve ... compared with triazoles alone." *Id.*

15. A network of uniform fungicide trials (UFTs), involved in annually evaluating fungicides since the 2003/04 season provided evidence suggesting a decline in sensitivity within the local *P. pachyrhizi* populations to multiple fungicides, since efficacy has been relatively low and apparently decreasing in recent years compared to previous reports. *Godoy et al.*, 51(5):407-421.
16. It was reported that in 2005/06 season, rust average control by DMIs was 90.3%. After only eight seasons, corresponding to 2012/13, DMI control was 52.0%, showing 42% control efficacy reduction. *Godoy, C. V. et al. Eficiência de fungicidas para o controle da ferrugem- asiática da soja, Phakopsora pachyrhizi, na safra 2012/13: resultados sumarizados dos ensaios cooperativos. Londrina:2013 (Circular Técnica, 9a) PR. Setembro, 2013. 7 p.* The reduction in Pp sensitivity to the fungicides tebuconazole and cyproconazole, with only 42 and 38% control, respectively, was also established. *Godoy, C.V.; Palaver, L. Ensaio cooperativo para avaliação da eficiência de fungicida no controle da ferrugem da soja, em Londrina, PR, na safra 2010/11. In: Reunião de pesquisa de soja da região central do Brasil. 32., 2011, São Pedro. Resumos. São Pedro, 2011.* In that same season, DMI + Qol mixtures did not show reduced efficiency yet; cyproconazole + azoxystrobin had 72% control and pyraclostrobin + epoxyconazole, 88% control. At this time, the mean control for the mixtures was 80%. *Id.* It is likely that the effectiveness was ensured by Qols, as the control mean for DMI was only 40%. *Id.* DMI and Qol fungicides act on only one specific site of thousands of biochemical reactions in the fungal cell. Therefore, they are vulnerable to fungal strain selection towards

sensitivity reduction or loss. The difficulty in controlling ASR with fungicides is becoming increasingly evident, proving the high fungal adaptability. *Godoy et al., Londrina:2013 (Circular Técnica, 9a) PR. Setembro, 2013; Schmitz, H. K. et al., Pest Management Science, 2013*. As an example, tebuconazole efficiency has been gradually reduced from 90% to 24% in ten seasons. *Id.* Some actions should be taken to make ASR chemical control reach 80-90% efficiency again, as in 2002/03 to 2008/09 growing seasons *Id.*

17. Data obtained from the studies conducted by Embrapa Soybean, showed a marked reduction, with an increase in the reduction every year, in the efficacy of soybean rust control. *Cláudia V. Godoy, "Changes in performance of SBR fungicides over the years and new management strategies adopted in Brazil, Embrapa Soybean, BR – slide presentation*. Yet, during those years almost 80% of the soybean rust control industry was using mixtures of systemic fungicides despite of the reduction in efficacy. *Id.*
18. The poor fungicide performances are possibly linked to reports of resistance to DMI and QoI fungicides. Schmitz et al. 2013. *Schmitz, H. K. et al., Sensitivity of Phakopsora pachyrhizi towards quinone-outside-inhibitors and demethylation-inhibitors, and corresponding resistance mechanisms. Pest Manag. Sci. 2013, 70:378-388.*
19. As such, the industry was faced with a problem in the resistance management of fungicidal combinations and was in dire need of a solution to address such problem of reducing efficacy of known fungicides towards soybean rust.
20. Recognizing the problem, i.e., decrease in the efficacy of combinations of various systemic fungicides, different approaches to maintain the efficacy of the systemic fungicides were undertaken.

Ch

21. Soybean seed was treated with combination of fungicides (carbendazim + thiram or fluquinconazole) followed by treatment with pyraclostrobin + epoxiconazole and trifloxystrobin + tebuconazole. *Godoy and Henning, Pesq. agropec. bras., Brasília, v.43, n.10, p.1297-1302, out. 2008.*
22. A premix of systemic fungicides (azoxystrobin and cyproconazole) was applied to different growth stages to control soybean rust. *Godoy, C.V. et al., Eficiência do controle da ferrugem asiática da soja em função do momento de aplicação sob condições de epidemia em Londrina, PR. Tropical Plant Pathology 34 (1) January - February 2009.*
23. "After 2007/2008, the decrease in efficacy became a general trend for DMI fungicides. The only exception was prothioconazole, which was launched in 2010, although it had been assessed since 2005/2006. Because of the reduced efficacy of DMIs, prothioconazole was launched as a mixture with trifloxystrobin." *Godoy, C.V. et al., Pesq. agropec. bras., Brasília, v.51, n.5, p.407-421, maio 2016.*
24. Combinations comprising new broad-spectrum Succinate Dehydrogenase Inhibitors (SDHIs) fungicides mixed with quinone outside inhibitors (QoIs), again both systemic fungicides, were launched onto the market in 2013. *Godoy, C.V. et al., Brazilian soybean pest management and threats to its sustainability. Outlooks on Pest Management – June 2015.* Triple combinations, comprising all systemic fungicides, were also tested for improvement in the efficacy combinations in controlling soybean rust. *Godoy, C.V. et al., Eficiência de fungicidas para o controle da ferrugem-asiática da soja, Phakopsora pachyrhizi, na safra 2014/15: resultados sumarizados dos ensaios cooperativos, p:1-6.*



25. The efforts highlighted above, in addition to various other approaches, to overcome the problems associated with decrease in efficacy of fungicidal combinations in treating soybean rust did not result in a favorable result. For example, treatment with fluquinconazol or with foliar fungicides of carbendazim + thiram delayed neither the appearance of first symptoms nor the evolution of the disease, in addition to lacking any benefit in the management of rust. *Godoy and Henning, v.43, n.10, p.1297-1302, 2008*. These studies also concluded that the addition of a foliar fungicide treatment regimen did not have a favorable influence on the standard known treatment regime of strobilurin + conazole fungicides for the control of soybean rust. *Id.*

26. The most effective strategy available to, and understood in, the industry – until disclosed in the instant application – was the use of double and triple combinations of demethylation inhibitors, quinone inhibitors, and succinate dehydrogenase inhibitors – all of which are systemic fungicides – for the control of soybean rust. However, since effective fungicides with a new mode of action are not readily available, the problems associated with 'decrease in fungicidal efficacy over the years' persisted due to unsuccessful attempts. The need to reverse such problems with the efficacy of systemic fungicides was well recognized in the field of fungicidal combinations.

27. The inventors of this application – including myself (Gilson Aparecido Hermenegildo de Oliveira) and my colleagues, Jaidev Rajnikant Shroff and Vikram Rajnikant Shroff – conducted studies set forth in the instant application to provide a long-awaited solution for the dreadful problem to the industry of fungicidal combinations for soybean rust control.

28. As mentioned above [in paragraph 7], most commonly used fungicides for soybean rust management, until publication of the instant application, belonged to demethylation

9

inhibitors (DMI) and quinone outside inhibitors (QoI), both of which are systemic fungicides. Although certain [double and triple] combinations of systemic fungicides were tested for control of soybean rust, a combination of systemic fungicides with multisite fungicides, such as copper fungicides, was never tested prior to the filing of the instant application.

29. Multisite fungicides, such as copper oxychloride, are intended to ensure the protection of plants before pathogen attack. They must be applied before the pathogens infect the plant, forming a protective barrier toxic for fungi and bacteria in plants. When applied to the surface of plant organs, exert toxic barrier preventing the penetration of fungi by inhibiting the spores germination process. *Syngenta. Boletim Técnico Priori Xtra. São Paulo: Sector Agro; 2004. p. 31.*

30. The pathogen for rust penetrates and colonizes the leaf tissue, forming necrotic lesions. Due to its penetrative nature, it has always been treated with systemic fungicides i.e. fungicides absorbed within the plant tissues. Multisite contact fungicides have not been recommended, or have been discouraged, from being used in rust control.

31. The instant application, for the first time, describes a fungicidal combination comprising a multisite contact fungicide such as copper fungicides and two systemic fungicides, a long-awaited solution to the problem of maintaining efficacy of the combinations towards controlling soybean rust. *Specification as originally filed, page 6.* The application discloses a fungicidal combination comprising at least one multisite contact fungicides (such as a copper fungicide), at least one first systemic fungicide (such as a succinate dehydrogenase inhibitor fungicide), and at least one second systemic fungicide (such as a quinone outside inhibitor fungicide or a demethylation inhibitor fungicide). *Id.*



32. Studies conducted by the inventors of the instant application showed that systemic fungicides effectively penetrate the dense canopy barrier of the infected leguminous plant while simultaneously not allowing the rust pathogen to move up the plant foliage. The contact protective copper fungicide component of the combination effectively penetrated the dense plant foliage, while the systemic fungicide component effectively prevented the rust pathogen from infecting the remaining portion of the plant effectively reducing the susceptibility of the plant towards the infection. This synergistic complementation was not seen when either the foliar protective fungicide or the systemic fungicide was individually used in isolation but was observed when the two fungicides were used in conjunction.

33. Prior to the filing of the instant application, and prior to the publication of the present application – as evidenced by the research studies cited above – there had been a general scientific prejudice in the state of the art against the use of multisite fungicides in soybean rust control program. The fungicidal combination as instantly claimed decisively marked an end to this scientific prejudice, to the extent that the scientific community took a dramatic turn immediately [and only] after the instant patent application was first published in the area of soybean rust control. The inventors of the instant application overcame this long held scientific prejudice by producing the claimed fungicidal combination.

34. In addition to addressing the long-standing need [of controlling soybean rust] in the industry, the synergistic complementation between the contact preventive copper fungicide and the combination of two systemic fungicides for the treatment and control of *Phakopsora* species of fungicides was found to be unexpected and surprising.

35. The understanding in the industry was that since systemic fungicides (DMI, QoI, or combination thereof) were indicated to be the best available for the control of soybean rust, there would not be any need for a multisite fungicide. Systemic fungicides, such as DMI and QoI, is taken up by a plant and is then translocated, within the plant system, thus protecting the plant from the attack of pathogenic fungi or limiting an already established infection. Whereas multisite fungicide must be applied before the pathogens infect the plant, forming a protective barrier toxic for fungi and bacteria in plants. Accordingly, due to the different modes of actions of systemic and multisite fungicides, they were never considered to be combined until after the publication of the instant application. Since the pathogen for soybean rust was locally systemic, there was no perceived benefit of adding a contact fungicide such as copper fungicides into the control program.

36. The research conducted by the inventors, and the subject matter disclosed and claimed, in the instant application, found that the addition of a multisite fungicide e.g. copper oxychloride to the combination of a demethylation inhibitor and a quinone outside achieved superior control of soybean rust. Copper oxychloride 588 SC was applied at 0.5 kg-L/ha. Pyraclostrobin 250 EC was applied at 0.32 L/ha, whereas metconazole 90 EC was applied at 0.55 L/ha. In these experiments, DAA/B/C meant days after treatment A, B and C respectively.

	Mixture	Copper Oxychloride		Difference in percentage control
		With out	With	
1	Pyraclostrobin + Metconazole @ 18 DAB	61.6	85.7	+ 24.1%

2	Pyraclostrobin + Metconazole @ 7 DAC	53.4	80.8	27.4%
3	Pyraclostrobin + Metconazole (AUDPC; % Control)	57.5	83.2	+ 25.7%

37. A marked reduction in severity of soybean rust and yield of soybean in treatments which were inclusive of a multisite contact fungicide in addition to the mixture of triazoles and/or strobilurins and/or SDHIs was observed. Such a reduction was unexpected and surprising given the understanding in the industry regarding the mechanism of action for contact fungicides, systemic fungicides, and mixtures thereof.

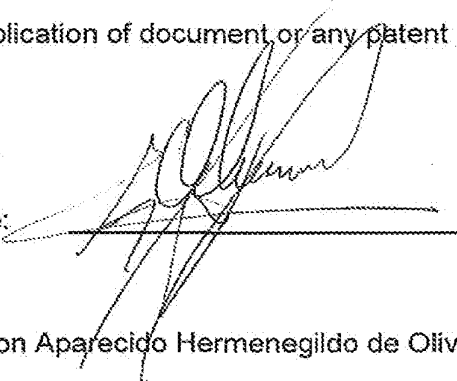
38. Only after the date of publication of the instant application, research scientists have started evaluating the combination of the contact fungicides. For example, in 2016, for the first time, studies were published regarding the role of copper oxychloride, chlorothalonil, mancozeb, copper sulfate, propineb, and fluazinam in addition to the long known mixture of triazoles and/or strobilurins and/or SDHIs for achieving a superior control of Asian soybean rust. *Godoy, C.V. et al., Eficiência de fungicidas multissítios no controle da ferrugem-asiática da soja, Phakopsora pachyrhizi, na safra 2015/16: resultados sumarizados dos ensaios cooperativos. P:1-7. See Table 3 and Table 4.*

39. The fungicidal combination as instantly claimed decisively marked an end to this scientific prejudice, to the extent that the scientific community took a dramatic turn immediately [and only] after the instant patent application was first published in the area of soybean rust control. The inventors of the instant application overcame this long held scientific prejudice by producing the claimed fungicidal combination.

40. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these



statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application of document or any patent resulting therefrom.

Signature: 

Print Name: Gilson Aparecido Hermenegildo de Oliveira

Date: 27 June 2019