EXHIBIT A-4

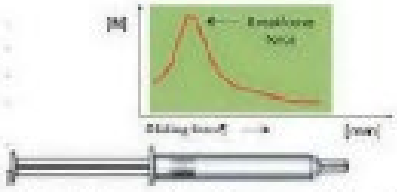
Invalidity Claim Chart of Reuter, alone or in combination with any of Sigg, Boulange, Lam, Scypinski, M Schoenknecht, Chacornac, Nema, D'Souza, Furfine, Badkar, Macugen, Eylea, Lucentis, Stewart, USP789 Hagen, Khandke, Wittland, Shams, Dixon, and/or Cormier against U.S. Patent No. 9,220,

Charted Reference:

Bruno Reuter and Claudia Petersen. "Die Silikonisierung von Spritzen: Trends, Methoden, Analyseverfahren," *T* (2012): 238-244. ("Reuter"), alone or in view of Sigg, Boulange, Lam, Scypinski, Metzner, Shah, Fries, Schoenk Nema, D'Souza, Furfine, Badkar, Macugen, Eylea, Lucentis, Stewart, USP789, Liu, Hioki, DC365, Hagen, Khan Shams, Dixon, and/or Cormier, render obvious claims 1-26 of U.S. Patent No. 9,220,631.

This claim chart is based on Regeneron's current understanding of the asserted claims, and Regeneron's investig Regeneron is not admitting to the accuracy of any particular construction. Regeneron reserves all rights to amend chart in light of any claim construction developments or any amendments to Novartis's infringement contentions contentions, should such developments occur or amendments be allowed. Further, as discovery is ongoing and R seek discovery from third parties regarding the references identified in Regeneron's invalidity contentions as wel prior art, Regeneron reserves the right to revise its invalidity contentions as appropriate in view of any ongoing d

The claim chart below identifies where each limitation of each asserted claim of the 631 Patent can be found in F provided below are exemplary, rather than exhaustive, and Regeneron reserves the right to rely upon any other p references. Where Regeneron identifies a portion of a reference's text, the identification should be understood as corresponding figure or diagram, and vice versa.

Claim Language	Corresponding Disclosure
[1.a-pre] A pre-filled … syringe	Reuter discloses a "pre-filled syringe." For example, see the following passages and/or figures, as well as all related d Ready-to-fill, i.e. sterile, prefillable glass syringes, are washed, siliconized packaged by the primary packaging manufacturer. They can then be filled pharmaceutical companies without any further processing. These days the prefillable syringes are made of glass and the trend looks set to continue. **Reuter at 1.** Although syringes and cartridges are always siliconized, this applies to a l vials and ampoules. On the container the siliconization provides a barrier tween the glass and drug formulation. It also prevents the adsorption or fo components on the glass surface. The hydrophobic deactivation of the sur improves the containers' drainability. In prefillable syringes and cartridges also performs another function. It lubricates the syringe barrel or cartridge the plunger to glide through it. Siliconization of the plunger stopper alone provide adequate lubrication. **Reuter at 1.**  Fig. 3: Extrusion force profile of a prefillable syringe. **Reuter at 3.**

Claim Language	Corresponding Disclosure
	Prefillable glass syringes are only manufactured from high quality type 1 l glass. **Reuter at 3.** To the extent Novartis alleges this limitation is not met by any of the disclosur have been obvious in view of Sigg, Boulange, Lam, Scypinski, Metzner, Shah, Schoenknecht, Chacornac, Nema, D'Souza, Furfine, Badkar, Macugen, Eylea, USP789, Liu, Hioki, DC365, Hagen, Khandke, Wittland, Shams, Dixon, and/o Exhibits A-1–A-3, A-5–A-13, B-1–B-3 and all references cited therein.
[1.a-pre] A … terminally sterilized syringe	Reuter discloses the need to terminally sterilize the syringe. It would have bee POSITA to terminally sterilize the prefilled syringes disclosed in Reuter to ens when administered to a patient. For example, see the following passages and/or figures, as well as all related d Ready-to-fill, i.e. sterile, prefillable glass syringes, are washed, siliconized packaged by the primary packaging manufacturer. They can then be filled pharmaceutical companies without any further processing. These days the prefillable syringes are made of glass and the trend looks set to continue. T siliconization of the syringe barrel is an extremely important aspect of the sterile, pre fillable glass syringes because the functional interaction of the siliconization and the plunger stopper siliconization is crucial to the efficie entire system. **Reuter at 1.** A POSITA would have understood the need to terminally sterilize the claimed would have had a reasonable expectation of success combining Reuter and Lar Metzner, Wittland, Hagen, Scypinski, and/or D'Souza in a way that satisfies th

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	To the extent this limitation is not expressly and/or inherently disclosed by Reu would have been obvious, even without resorting to the disclosures of any othe it was within the common knowledge of persons of ordinary skill in the art, an according to known methods, to achieve predictable results. In addition, the 631 Patent fails to disclose a new process for terminal steriliza explains "a careful balancing act is required to ensure that while a suitable leve carried out, the syringe remains suitably sealed, such that the therapeutic is not Patent at 1:31-36. The 631 Patent says that the sterilization it discloses may be methods, such as by using VHP or EtO, but no details are provided regarding t process itself. 631 Patent at 9:49-54 ("As noted above, a terminal sterilisation p to sterilise the syringe and such a process may use a known process such as an (EtO) or a hydrogen peroxide (H2O2) sterilisation process. Needles to be used may be sterilised by the same method, as may kits according to the invention." description in the 631 Patent only sets forth desired results – how long the syri the Sterility Assurance Level, the alkylation of the product, and the amount of remaining – but does not detail the steps to achieving them. *See e.g.*, *id.* at 9:55 631 Patent does not provide any details regarding the known sterilization meth those methods were known in the art and thus render this claim limitation obvi A POSITA would have known that terminal sterilization of prefilled containers packaging is one way to sterilize the device and maintain a low bio-burden and contaminants. A POSITA also would have known that terminal sterilization is range of solutions, including those that are temperature, oxidation, or radiation Moreover, if Novartis contends that Reuter does not disclose the claimed limit renders this limitation obvious in view of numerous prior art references. A pers in the art would have been motivated to combine the teachings of Reuter with Metzner, Wittland, Hagen, Scypinski, and/or D'Souza, and would have had a r expectation of success in doing so, at least because these references are in the s Moreover, the references teach the benefits and advantages of applying termin techniques, as can be seen in the excerpts below. It further would have been an

Claim Language	Corresponding Disclosure
	choice. Such a person likewise would have understood that such combination w nothing more than a simple substitution or combination of known elements and application of known techniques, to achieve predictable results. For example, see the following passages and/or figures, as well as all related d Objects used in medical applications are generally sterilized before use. St be accomplished by a variety of methods including, e.g., steam sterilizatio sterilization, gas sterilization (e.g. with ethylene oxide), and chemical ster However, these treatments cannot be used for objects containing pharmac compositions because their active ingredients are typically sensitive to the steam and gas sterilization are generally performed at high temperatures (a 55°C or higher) that damage certain active ingredients in pharmaceutical c Similarly, the agents used for radiation or chemical sterilization generally damage to the active ingredients. Consequently, pharmaceutical compositi generally sterilized by an alternative method, e.g. by filtration, and then pa separately sterilized objects. Because of the complexity of this process, it also ensure the sterility of the surfaces of the objects. In many circumstances it would be advantageous to sterilize the surfaces o in order to reduce the risk of contamination during subsequent handling. F there is an increased risk of endophthalmitis after intraocular injection if th syringe used for injection is not sterilized. Thus, there remains a need for e cost-effective methods of surface-sterilizing objects containing ethylene-o temperature-sensitive compounds, such as biological molecules, without a adverse effect on their activity or integrity. **Lam at 1:14-32** The invention relates to methods for surface-sterilizing objects containing oxide-sensitive, temperature-sensitive compounds, such as biological mol invention is based, in part, on the surprising discovery of ethylene-oxide-b

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