

Exhibit 1003

Coalition For Affordable Drugs V. HHS

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(56) Documents Cited:
EP 0480054 A1 **WO 2002/009707 A1**

(58) Field of Search:
INT CL⁷ **A61K, A61P**
Other: **CAS-ONLINE, EPODOC, PAJ, TXTE & WPI**

(54) Abstract Title: **Sub-lingual fentanyl formulation**

(57) An pharmaceutical formulation comprising (i) fentanyl or pharmaceutically acceptable salt thereof, (ii) water and (iii) a polar organic solvent, wherein the said polar organic solvent is available in a sufficient amount to enhance the solubility of the fentanyl or salt thereof in the water. The resulting solution is for use as a sub-lingual spray - preferably delivered by means of a pump spray device.

GB 2 399 286

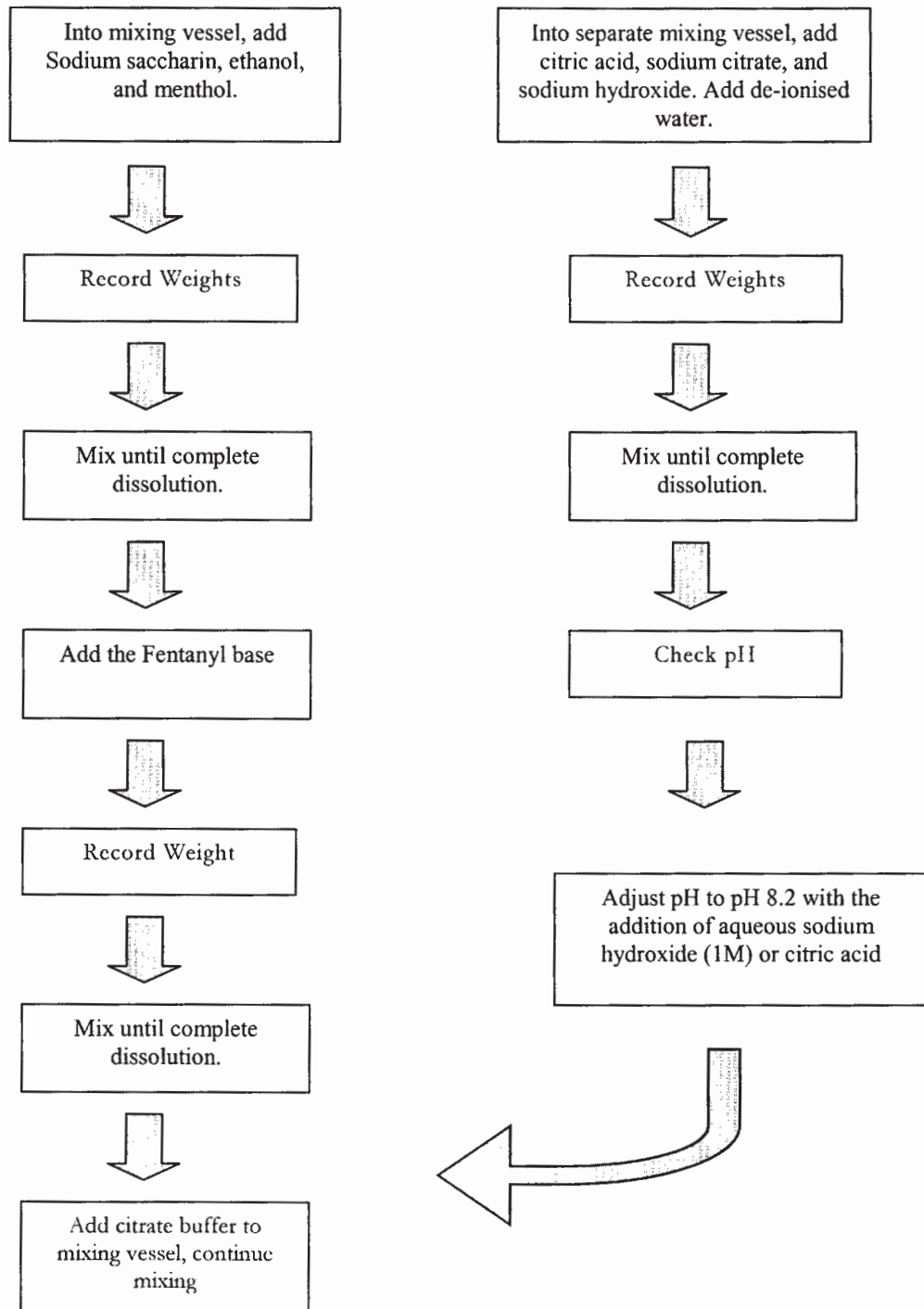


Fig. 1

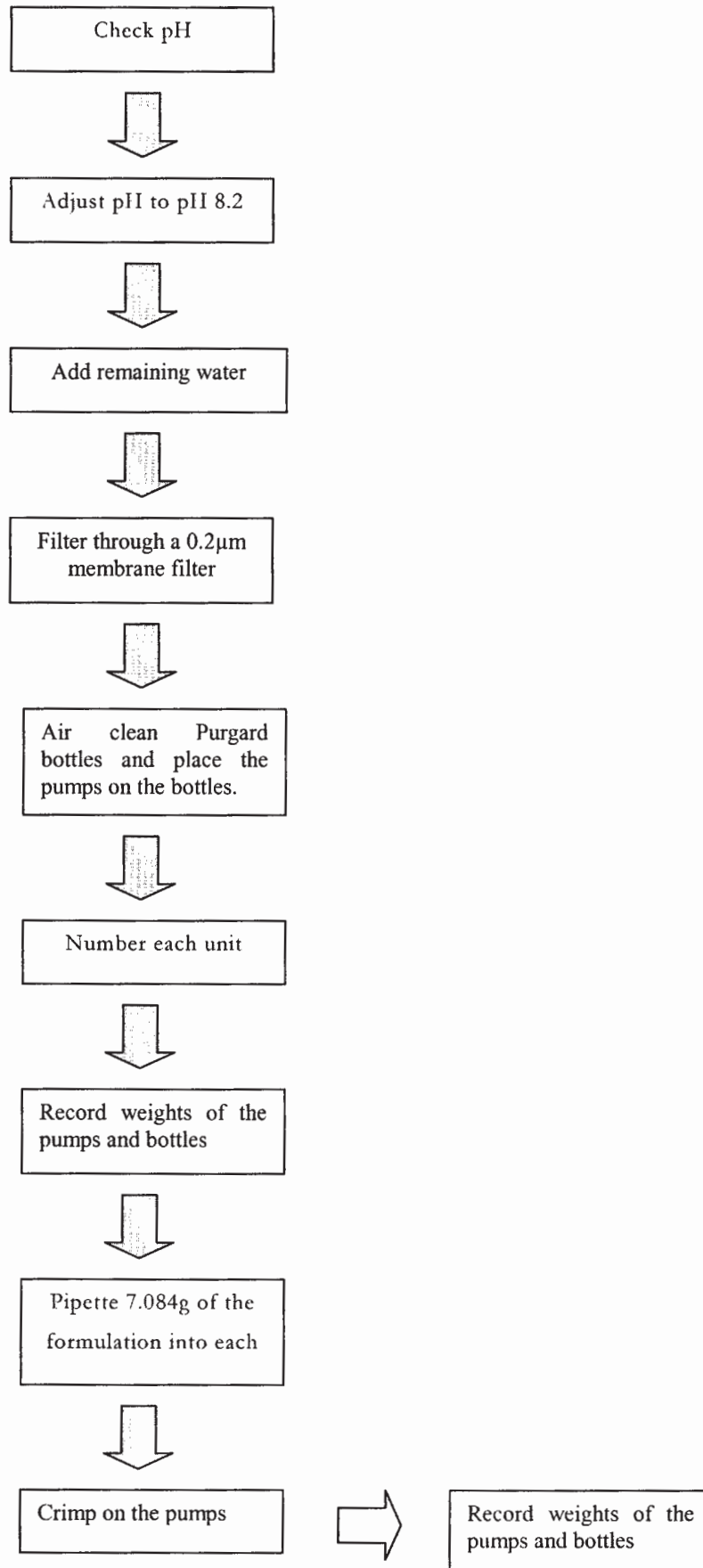


Fig. 2

Novel Compositions

This invention relates to formulations of fentanyl, especially pump spray formulations suitable for sublingual delivery.

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Fentanyl is a narcotic alkaloid, which has been used for many years as an anaesthetic and an analgesic, especially in the treatment of moderate to severe pain. Whilst undoubtedly effective for pain relief, and especially in the treatment of pain which is refractive to other treatments, there are a number of issues of clinical management
10 associated with the use of fentanyl in therapy.

Foremost amongst these issues is the potential for serious side effects with fentanyl. It has a much higher potency than commonly known narcotics and therefore it is necessary to ensure that it is being used within the established therapeutically
15 effective range and to monitor patients for evidence of self medication at greater than the recommended amount. Overdosage with fentanyl can lead to a number of undesirable and indeed life-threatening side effects, predominantly hypoventilation and respiratory depression.

20 Due to the nature of the conditions being treated, it is much desired that the onset of analgesia occurs as soon after dosage as is compatible with safety parameters. Furthermore delay in onset of action may prompt the patient to take another dose with consequent risk, as already explained above, of overdosage.

25 A number of routes of administration of a medicament can be associated with rapid onset of action. For example, International Patent Application WO90/07333 (Riker Labs) described aerosol formulations of fentanyl, which are adapted for inhalation. However Riker's formulations suffer disadvantages such as their use of hydrofluorocarbon propellants and delivery effected by metered dose inhalers. In
30 the case of the former the disadvantages include high velocity which results in 'bounce back' on administration to the front of the mouth, cold sensations on administration, the risk of inhalation and for the latter, careful co-ordination of

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