DSP 8.11.89

- assume Johnson melted initial aim

# AGENDA FOR FVIII IMPROVED STABILITY AND YIELD

(Possible actions which are jointly agreed between PFC, HQ LAB & SEBTS)
CVP, PF & DSP 10.11.89

(0) PRODUCT(S) SPECIFICATION(S)

(1) Improved Stability of FVIIIC

1.1 Improved stability of FVIIIC in terminal heating
1.2 " " " " in process
1.3 " " " " during collection/storage/transport

(2) IMPROVED STABILITY OF vWF

(3) ASSAY METHODOLOGY

3.1 FVIIIC - "clotting" 1-st; 2-st; chromogenic
3.2 FVIIIC-Ag - ELISA, other? MB - current work at PFC Coag-
3.3 FVIIIC - chain structure Weinstein; blotting; other?
3.4 vWF Ag; RiCof; subunits; other? Collagen binding Assay - need aggregometer
3.5 Contaminants - FIB; FN; (other) Laurell Rockets
3.6 Water content by Infra-red spectroscopy
3.7 Ionized $Ca^{++}$ (interference by $M^{++}$?)
3.8 Redox potential; $O_2$ content? Ethanol (HL).
3.9 Other analytes (Detergent, Solvent, Glycerol etc) aka Triton
3.10 FII/Thrombin and other clotting factors; aggregates by HPLC

(4) EMPIRICAL APPROACH

4.1 Add stabilizers (see Appendix 1)
4.2 Remove de-stabilizers (see Appendix 2)
4.3 Differential partitioning of FVIII & de-stabilizers

(5) THEORETICAL APPROACH

5.1 Literature and Patent Survey + CDA - technology disclosures
5.2 Personal contacts including visits etc.
5.3 Develop theoretical framework to explain past results and predict future performance

* (6) VIRAL INACTIVATION

- 6.1 Dry heat (freeze drying and water content)
- 6.2 Wet heat
- 6.3 Irradiation (γ & UV; wet, dry and frozen) ? Bruce
- 6.4 Solvent/detergent
- 6.5 Chemical (nuclease; psoralen) Bruce
- 6.6 Virology assays (T/C etc) and models Phage T4
- 6.7 Combinations of above with separation steps

(7) MISCELLANEOUS ITEMS

- 7.1 Acquire multiple vial panels of competitors products; in-process samples
- 7.2 Small scale and pilot scale models
- 7.3 Develop other separation steps
- 7.4 Artificial depleted substrate(s)
- 7.5 Pyrogen

(8) RESOURCES REQUIRED

- 8.1 People
- 8.2 Materials
- 8.3 Equipment
- 8.4 Costs

(9) ORGANISATION

- 9.1 Communication
- 9.2 Time scale
- 9.3 Priorities