Drug Information for PET Radiopharmaceuticals

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Historical Background: Development of USP Dispensing Information (the USP DI)

- **1970** The United States Pharmacopeial Convention adopted a resolution to increase information content useful to pharmacists and others.

- **1970-1975** The Subcommittee on Posology and Related Information introduced into many USP XIX drug monographs a section entitled *Dispensing Information*.

- **1975-1980** The Subcommittee greatly expanded the amount and kinds of information in the DI database.
Development of USP DI (cont’d)

- The DI database focused on information that would enhance the safe and effective use of drugs once they were prescribed, including drug use information relating to dispensing, administration, monitoring, and patient consultation.

- 1980  1st edition USP DI as a separate book
- 1983  USP DI grew to two volumes
- 1989  USP DI grew to three volumes

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USP DI Monograph Contents

Similar to a package insert, but additional information:

- off-label indications (originally established by expert consensus but later involved review of published literature with evidence tables)
- use in pregnancy, breast-feeding, pediatric, geriatric
- drug interactions, alterations in lab values
- side effects (based on seriousness, frequency, effect on life-style and patient concern)
- patient consultation/advice for the patient
- usual doses in special groups (pediatric, geriatric)
Radiopharmaceuticals in USP DI

- 1980 - no radiopharmaceuticals in this 1st USP DI
- 1984 - first appearance of radiopharmaceutical monographs in the USP DI (N = 13)

- Cyanocobalamin Co 57
- Gallium Citrate Ga 67
- Iodohippurate I 131
- Sodium Chromate Cr 51
- Sodium Iodide I 123
- Sodium Iodide I 131
- Sodium Phosphate P 32
- Sodium Pertechnetate Tc 99m
- Technetium Tc 99m Albumin Aggregated
- Technetium Tc 99m Sulfur Colloid
- Technetium Tc 99m Pyrophosphate
- Technetium 99m Human Serum Albumin
- Xenon Xe 133
Radiopharmaceuticals in USP DI (cont’d)

- 1985 – 12 more radiopharmaceutical monographs were added, for a total of 25

  - Ferrous Citrate Fe 59
  - Indium In 111 Pentetate
  - Iodinated Albumin I 131
  - Krypton Kr 81
  - Selenomethionine Se 75
  - Thallous Chloride Tl 201
  - Technetium Tc 99m Disofenin
  - Technetium Tc 99m Gluceptate
  - Technetium Tc 99m Medronate
  - Technetium Tc 99m Oxidronate
  - Technetium Tc 99m Pentetate
  - Technetium Tc 99m Succimer
18th Ed. USP DI, 1998: 50 radiopharmaceuticals including 2 non-commercial PET radiopharmaceuticals

Ammonia N 13
Chromic Phosphate P 32
Cyanocobalmin Co 57
Ferrous Citrate Fe 59
Fludeoxyglucose F 18
Gallium Citrate Ga 67
Indium In 111 Capromab
Indium In 111 Oxyquinoline
Indium In 111 Pentetate
Indium In 111 Pentetreotide
Iobenguane I 123
Iobenguane I 131
Iodinated I 125 Albumin
Iodinated I 131 Albumin
Iodohippurate Sodium I 123
Iodohippurate Sodium I 131
Iofetamine I 123

Krypton Kr 81m
Rubidium Rb 82
Samarium 153 Lexidronam
Sodium Chromate Cr 51
Sodium Iodide I 123
Sodium Iodide I 131
Sodium Pertechnetate Tc 99m (ophthalmic)
Sodium Pertechnetate Tc 99m
Sodium Phosphate P 32
Strontium Chloride Sr 89
Technetium Tc 99m Albumin
Tc 99m Albumin Aggregated
Tc 99m Albumin Colloid
Technetium Tc 99m Bicisate
Technetium Tc 99m Disofenin
Technetium Tc 99m Exametazime

Technetium Tc 99m Gluceptate
Technetium Tc 99m Lidofenin
Technetium Tc 99m Mebrofenin
Technetium Tc 99m Medronate
Technetium Tc 99m Mertiatide
Technetium Tc 99m Oxidronate
Technetium Tc 99m Pentetate
Technetium 99m Pyrophosphate
Tc 99m Pyro/Trimeta Phosphate
Technetium Tc 99m Sestamibi
Technetium Tc 99m Succimer
Technetium 99m Sulfur Colloid
Technetium Tc 99m Teboroxime
Technetium 99m Tetrofosmin
Thallous Chloride Tl 201
Xenon Xe 127
Xenon Xe 133

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USP DI – Transitions

- 1998  USP Board of Trustees sold the USP DI database and licensed the USP DI trademark to Thompson Corporation, with continued involvement of USP expert committees.
- 1999  19th edition USP DI was published by Thompson MICROMEDEX.
- 2001  Radiopharmaceutical monographs were “excluded” from the printed USP DI; they were only available to paid subscribers via an internet website.
USP DI – Transitions

- 2004  24th Edition USP DI was the final edition; MICROMEDEX discontinued further publication of USP DI

- In this last edition, there were 62 radiopharmaceutical monographs, including 9 non-commercial PET radiopharmaceuticals:

  - Ammonia N 13
  - Fludeoxyglucose F 18
  - Fluorodopa F 18
  - Mespiperone C 11
  - Methionine C 11
  - Raclopride C 11
  - Sodium Acetate C 11
  - Sodium Fluoride F 18
  - Water O 15

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What’s Been Happening at USP?

- Former Radiopharmaceuticals Information Expert Committee chair Carol Marcus, PhD, MD worked for 2+ years to develop a new information monograph template

- In fall 2007, USP legal staff agreed that the new monograph template avoided copyright issues vis-à-vis MICROMEDEX

- Re-start up of committee work was curtailed, primarily due to a vacant USP staff position for this committee, financial considerations, and the subsequent economic downturn

- In fall 2008, USP decided to dissolve the Radiopharmaceutical Information Committee at the end of the current cycle
Currently Available Drug Information for PET Radiopharmaceuticals

- Monographs in USP-DI 2004
  - Ammonia N 13
  - Fludeoxyglucose F 18
  - Fluorodopa F 18
  - Mespiperone C 11
  - Methionine C 11
  - Raclopride C 11
  - Sodium Acetate C 11
  - Sodium Fluoride F 18
  - Water O 15

- NDA Product Package Inserts
  - Ammonia N 13  [Feinstein]
  - Fludeoxyglucose F 18  [Weill; Feinstein]
  - Rubidium Chloride Rb 82 Injection  [Bracco]
Whither PET Drug Information?

- If all PET Radiopharmaceuticals will be NDA:
  - basic drug information will be contained in the product package inserts; but drug information is still needed for “off-label” uses, etc.

- If [at least some] PET Radiopharmaceuticals continue to be ‘compounded’ per 1997 FDAMA:
  - there continues to be a need for a source of readily available, up-to-date drug information for non-commercial PET radiopharmaceuticals
Proposal for USP Action

1) Re-write and update USP-DI 2004 drug information for non-commercial PET radiopharmaceuticals:
   - Fluorodopa F 18
   - Mesperone C 11
   - Methionine C 11
   - Raclopride C 11
   - Sodium Acetate C 11
   - Sodium Fluoride F 18
   - Water O 15

2) Develop new information for non-commercial PET radiopharmaceuticals already in USP:
   - Carbon Monoxide C 11
   - Flumazenil C 11
Proposal for USP Action (cont’d)

3) Re-write and update USP-DI 2004 drug information for commercial PET radiopharmaceuticals, especially related to ‘off-label’ uses and other information not included in the package insert

- Ammonia N 13
- Fludeoxyglucose F 18
- Rubidium Chloride Rb 82 Injection
Proposal for USP Action (cont’d)

4) Develop new drug information for non-commercial PET radiopharmaceuticals not yet in USP but which have been formally identified for development of a USP monograph:

   Fluorodeoxythymidine F 18       Iobenguane I 124
   Fluoromethane F 18              Oxygen O 15

5) As other non-commercial PET radiopharmaceuticals are identified for development of a USP monograph, concurrently develop new drug information for each
Proposal for USP Action (cont’d)

- this drug information could be considered to be a section of the drug [standards] monograph, similar to the Dispensing Information section of many USP drug monographs in the 1970s.

- create a website for drug information for PET radiopharmaceuticals
  - information would be readily available
  - information would be easily updated/revised
  - access limited to USP subscribers via password
Conclusion

- Until its recent discontinuation, USP DI was a well recognized and widely used source of radiopharmaceutical drug information.

- There is currently an unmet need for drug information for non-commercial PET radiopharmaceuticals, which will continue unless/until all PET drugs are NDA and thus have product package inserts; however, there is still a need for drug information for “off-label” uses, etc.

- It has been proposed that USP develop drug information as a section of PET drug monographs and maintain such drug information on a subscriber website.