Determination of equivalence
相同产品的判定

Why determine equivalence?
为什么要判定相同产品？

To check that: 目的在于核查

- (i) an existing FAO/WHO specification is applicable to another manufacturer's product;
  现有的FAO/WHO规格是否适用于其它生产厂商生产的产品

- (ii) the other manufacturer's products do not pose additional or greater hazards, compared with the product on which the existing specification is based.
  和现有规格的基础产品相比，其它生产者生产的产品不具额外或更大的危险性

What is equivalence?
什么是相同产品？

- Another manufacturer's TC/TK or formulation is considered to be no worse* than the products on which the existing specification is based.

  其它生产者生产的原药/母药或制剂被认为不比现有规格的基础产品差

  (*an equivalent product could be better but this is difficult to prove and therefore is not considered)

  （一个相同产品可能更好，但很难证明，因此不予考虑）
- That is, no additional or greater hazards are expected to be involved in handling and use.

  在操作和使用时，不应具有额外的或更大的危险性

  Note: equivalent formulations may not be intended for the same applications and may not provide equal performance in use.

  注意：相同的制剂可能使用方法并不相同，因此使用时的表现可能不同

Equivalence determination
相同产品的判定

- Requires access to confidential data from both manufacturers.
  要求有权使用两个生产者的保密资料
- The rules are simple, but expert opinion is often required to make a judgement and different information may available to different organizations.
  规则简单，但对专家的意见往往需要做出判断，并且不同组织所拥有的信息资料并不相同
  - so JMPS conclusions may differ from those of other organizations, such as registration authorities.
    所以JMPS的结论可能与其它组织的不同，如登记管理部门

Data requirements
资料要求

- The original specification must be based on a “full” data package:

  最初的规格必须基于“完整”的数据资料

  - not a limited data package; because a full data package provides the “reference profiles”.

    不是有限的数据资料；因为完整的数据资料提供了“参考概述”

- Subsequent manufacturers’ products may be supported by a limited data package.

  后来生产者生产的产品可以用有限的数据资料来支持

“Full data package”
完整的数据资料

- Confidential and non-confidential data:
  保密和非保密性资料
  - manufacturing process and impurity profiles;
    生产过程和杂质资料
  - “complete” toxicology profile;“完整”的毒理资料
  - “complete” ecotoxicology profile;“完整”的生态毒理资料
  - efficacy from WHOPES and/or national registration;
    从WHOPES和/或国家登记机构获得的药效结果
  - physical and chemical properties of active ingredient;
    有效成分的物理和化学性质
  - additional information to support specification clauses and limits which differ from the guidelines.用于支持与指南不同的规格条款和限量的额外资料

“Limited data package”
有限的数据资料

- Confidential and non-confidential data:保密和非保密性资料
  - manufacturing process and impurity profiles; 生产过程和杂质概述
  - acute toxicology* data; 急性毒理数据
  - possibly some ecotoxicology data; 或许一些生态毒理数据
  - national registration information; 国家登记资料
  - information to support proposed changes to existing specification clauses and limits. 用以支持对现有规格的条款和限量进行修改的资料

* requirements under review重新审查的资料要求

Criteria for equivalence
相同产品的标准

- 1. Does the “new” product comply with the existing specification?
  “新”产品符合现有规格吗？
- 2. Does the “new” product contain higher levels of any impurity (relevant or non-relevant), based on a comparison of manufacturing limits?
  和生产限量比较，“新”产品含有更高量的杂质（相关的或非相关的）吗？
- 3. Is the “new” product more hazardous or does it pose any additional hazard, compared with the “original” material?
  和“最初”的物质比较，“新”产品更危险或可能导致额外危险吗？

Purity/impurity profiles (manufacturing limits data)
纯度/杂质组成（生产限量资料）

- Minimum active ingredient content, TC/TK.
  有效成分最低含量，原药/母药
  - If the specification is “minimum 960g/kg”, does the “new” material comply with this?
    如果规格规定“大于960克/千克”，“新”物质符合吗？
  - Higher minimum concentrations are automatically equivalent.
    高于最低含量的产品，被自动认为是符合相同条件的
- Impurities杂质
  - Non-relevant impurities should not exceed reference profile limits by >50% or >3 g/kg, whichever is the greater.
    非相关杂质的增加不应>50％参考限量或>3克/千克
  - Lower concentrations are automatically equivalent.
    低于参考限量的产品，被自动认为相同
  - No new relevant impurities and specified relevant impurities within existing limits.
    没有新的相关杂质发生，而特定的相关杂质含量低于现有限量

Purity/impurity profiles
纯度/杂质组成

- New or higher-concentration non-relevant impurities may be accepted as equivalent in some cases.

  有时新的或高含量的非相关杂质可能会作为相同产品被接受
- Higher concentrations of relevant impurities may also be accepted as equivalent, but not if the “10% increase in hazard limit” is exceeded.

  较高含量的相关杂质可能也会作为相同产品被接受，但不得超过“10％的危险限量”
- In both cases, only if the toxicology data show no increase in hazard and no new hazards.

  以上两种情况，只有毒性资料显示危险性没有增加及没有新的危险性，才可以被接受
  - Note: the reference profiles are not changed by extending the specification to equivalent products.

    注意：参考含量不会因为相同产品规格的不同而改变

Toxicology and ecotoxicology profiles
毒理学和生态毒理学资料
(data from batches with “normal” purity/impurity profiles)
（“常规”批次的纯度/杂质数据）

- Toxicology results within a factor of 2 of (or the dosage intervals if greater), or no change in assessment from those in the reference profile.
  毒理结果在基准的2倍以内（或如果增大在剂量间隔内），或与基准的评估没有变化
- Ecotoxicology results within a factor of 5 (or the dosage intervals if greater) of those in the reference profile.
  生态毒性结果在基准？？的5倍以内（或如果增大在剂量间隔内）

Doubtful and missing data?
不确定和缺少的数据？

- Manufacturer is asked for an explanation or further data, if already available.
  会要求生产者解释或提供进一步的资料，如果有资料
- Seek advice of WHO/PCS toxicologists.
  征求WHO/PCS毒理专家的意见
- If doubts/omissions are not significant, recommend equivalence, otherwise recommend non-equivalence.
  如果不是特别显著的不确定/省略，建议为相同产品，否则建议为非相同产品
- Explain decisions in the evaluation.
  在评估中说明决定

Future 将来

- Some special formulation types (such as long-lasting insecticidal nets, LN), which may involve different technologies, may not conform to the usual extension and equivalence criteria.

  一些特殊的剂型（如长久杀虫网，LN）,会涉及到不同的技术，可能不符合常规的相同产品判定标准
- Toxicology data requirements are under review. In future, may include data from *in vitro* mutagenicity tests on the "new" TC/TK.

  毒理数据的要求在进行重新审查。将来，可能会要求"新"原药/母药提供其体外致突变试验资料

Summary总结

- Equivalence does not mean that two TCs/TKs are identical but that, on the basis of the information available, the "new" material is not worse than the material on which the specification was based.

  相同产品并不意味着两个原药/母药是完全相同的，只是根据现有的资料，"新"物质不比原有规格的基础产品差。

- Determination of equivalence requires careful comparisons of many data. Experience and good judgement in several scientific disciplines are required.

  相同产品的判定要求对许多资料进行仔细地比较。要求具有多个学科的经验和良好的判断力。