Adrenaline base and tartrate – DMF filing in Brazil

During CPhI 2019 in Frankfurt the Brazilian Health Authority, ANVISA invited stakeholders to their lecture and dialogues “APIs and the New Brazilian Regulation”.

The below brief summary outlines the new guidance for filling DMFs (DIFA) in Brazil as well as some API GMP issues. In respect to our Adrenaline base and tartrate we filed the CEP corresponding DMFs following the below option b) plus notification of availability of a CEP.

DMF (DIFA)

- Brazilian abbreviation **DIFA** is a synonym for ASMF, DMF, AIMF
- A new ANVISA DMF procedure will be implemented in 1st quarter 2020; only applicable for new applications; old (pending) procedures still follow the “old” procedure
- DIFA will have the same structure and content as an EDMF; split in Applicants Part and Restricted Part
- Accepted DIFA languages: English, Portuguese, Spanish
- Filing per PDF; upload to ANVISA gateway max. 25 MB per file; pre-registration to the gateway (so far only in Portuguese available) is required; CD; eDIFA is under development.
- Submission approach of the various DIFA parts as in EU: AP + RP to authorities; AP to customer

- DIFA filing options:
  a) full API dossier (DIFA AP plus RP) as part of the FDF dossier
  b) DIFA procedure like an EDMF procedure in conjunction with an MAA/MAV
  c) “Expression of interest”: DIFA Submission without any MA reference; stand-alone review and approval

- ANVISA didn´t tell about their review period, but deficiency letter response time will be 120 days.
- DIFA revision procedure is analogous to CEP; very similar change classification guideline is established
- Each API grade and/or API-polymorph needs an individual DIFA; several grades/morphs in 1 DIFA is impossible!

GMP

- ICH Q7 is the general framework
- Starting material/critical intermediate justification and discussion similar to EU: When does a DMF/GMP start?
- ANVISA´s options of GMP clearance of API manufacturers:
  a) Site was successfully inspected by a Recognized Authority
  b) Risk assessment/desk audit
  c) On-site Inspection

- ANVISA will set up an own database containing their GMP certificates/approvals