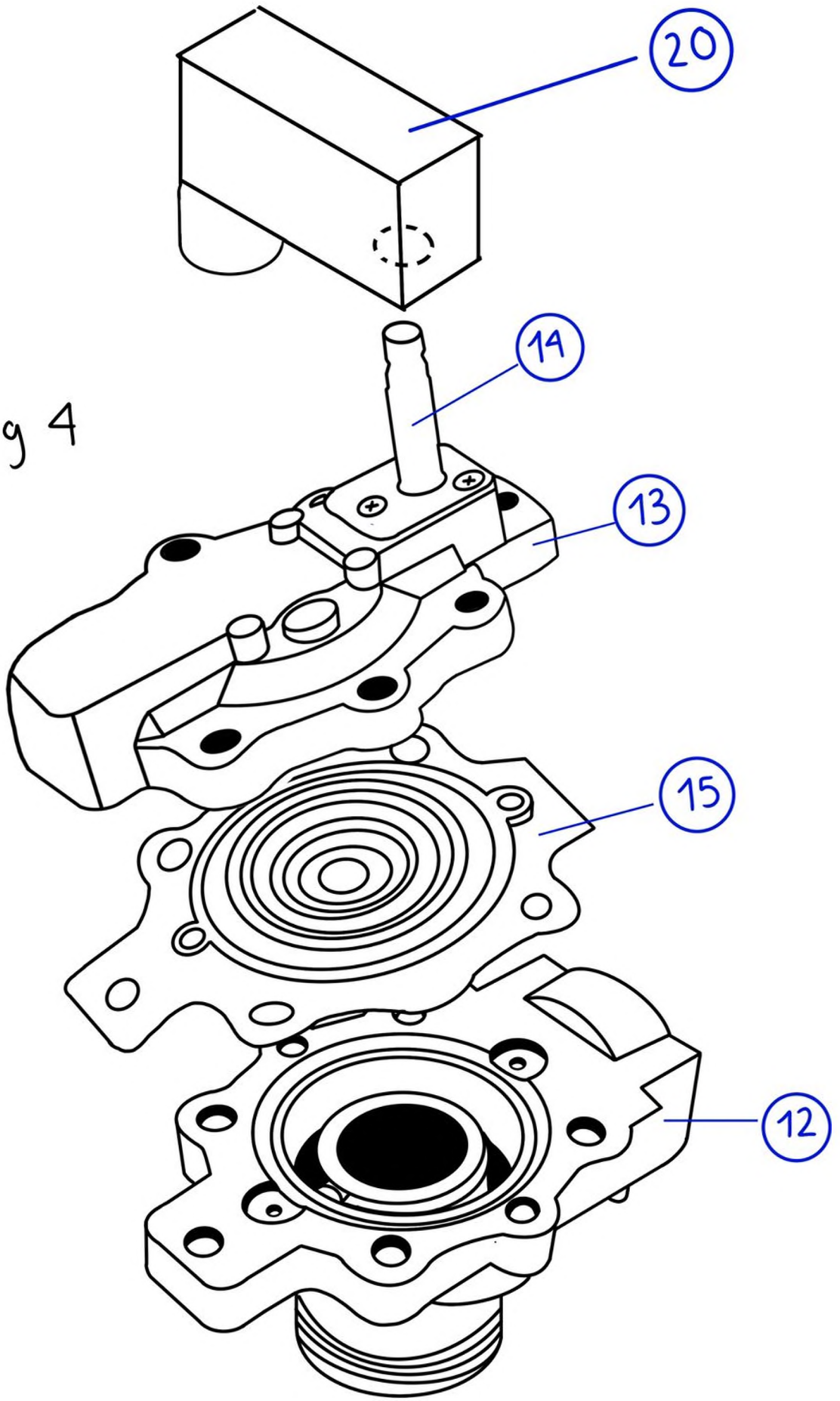Fig 4